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EDITORIAL

THE sixteenth Annual Report of the Ministry of Health has just been issued and contains tables showing that the decline in the incidence and death-rate from tuberculosis is being maintained in England and Wales. The total number of deaths from tuberculosis in 1934 per million population was 763, the lowest death-rate for tuberculosis ever recorded for England and Wales. Of these deaths 635 were from the pulmonary and 128 from the non-pulmonary form of the disease. In 1930 the corresponding figures were 739 and 159, and in 1925 they were 833 and 206.

This steady decline does not appear to be affected by any new treatment or discovery. The discovery of the tubercle bacillus and of tuberculin, and the development of treatment by pneumothorax, by sanocrysin or by surgical methods have revolutionised the treatment of tuberculosis. A sanatorium is no longer a place where the patient is over-fed and left to lie in a draught. Look at the tables of death-rates, however, and one sees a steady decline, and it is impossible to say here is a big fall in death-rate coinciding with the use of this or that new treatment. The only outstanding interruption in the decline was during the years of the war. The figures per million living in England and Wales were as follows:

1914	988	1916	1,046
1918	1,165	1919	918

The influenza epidemic of 1918 and 1919 had some effect on the tuberculosis death-rate, but much less than is generally supposed. Deaths from influenza, in England and Wales, rose from 174 in 1917 to 3,024 in 1918. It would appear that this decline in the tuberculosis death-rate and,

indeed, in the general death-rate of the population, is chiefly due to progress of civilization bringing with it better conditions of living, and that if this progress is interrupted, as by a war, the death-rate rises.

Those of us who treat the individual consumptive should not be disheartened by these reflections, for there is no doubt that modern treatment does prolong the life of the patient in many cases and not infrequently effects a cure.

It will be interesting to see whether treatment becomes perfected before the day when there are no patients to treat.

PROBLEMS IN APPLIED MEDICINE

WHY DO RELAPSES OCCUR IN PULMONARY TUBERCULOSIS?

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It seems inevitable that the actual treatment of the active phases of chronic pulmonary tuberculosis must remain in the hands of those physicians who are in charge of tuberculosis institutions. Vitally important though this part of the handling of any case of chronic pulmonary tuberculosis is, it must be remembered that the life of a successfully treated case may be anything from five to fifty years, and that, of that period, he will spend a comparatively short time under institutional treatment. Success may, in a few cases, be wholly due to the extreme efficiency of the institutional treatment, but in the majority of successful cases it is to be ascribed to efficient pre- and post-institutional handling, and thus lies in the hands of the general practitioner and/or of the dispensary physician. The treatment of the active phases is often simple and straightforward. The general handling of any case after the apparent arrest of activity is always difficult. Its success depends in the main on the prevention, or early recognition and prompt treatment, of relapse. Relapse or reactivity is one of the outstanding clinical features of chronic pulmonary tuberculosis, and so I propose, in this paper, to try to classify and define the different forms of relapse in this disease and to suggest some formal methods of procedure for their prevention, early recognition, and treatment.

There are three forms of relapse. They differ completely in their pathology, symptomatology, recognition, prevention, and treatment.

They may be summarised thus:

(1) Relapse due to the deposition of an entirely fresh lesion in a hitherto undiseased portion of the lung—*New lesion relapse.*

(2) Relapse due to spread by contiguity of a hitherto quiescent or arrested lesion—*Spread relapse.*

(3) Relapse due to changes taking place in an apparently arrested lesion, unaccompanied by actual area spread of disease—*Late relapse.*

1. New Lesion Relapse.

Pathology.—In a case that has been so treated that the active lesion has been brought to a state of quiescence or arrest, without there occurring any adverse change in that lesion, an entirely fresh lesion may be deposited in another part of the same or the other lung. The new lesion in its early stages is of the nature of a simple inflammatory allergic reaction round a new deposit of tubercle bacilli. Whether this new deposit of bacilli is of endogenous or exogenous source, or whether it is deposited in the lung by the blood stream or is inhaled, need not concern us here. Depending on the size of the infecting dose, the intensity of the allergic reaction and the immunity of the patient, one of two things may happen. Either the newly deposited tubercle bacilli will be destroyed, the allergic reaction subside, and the lesion disappear, to leave an infinitesimal scar, or as the allergic reaction subsides the tubercle bacilli multiply and an active spreading tubercular lesion results. These new lesions may be deposited in any part of either lung, but from their apparent localisation in straight X-ray films, I believe that the lung tissue near to a pre-existing focus of disease is their favourite site. That is to say, they are more common in that part of the organ which, by virtue of its proximity to an existing focus, possesses a higher degree of allergy than the more distant parts.

Ætiology.—There appears to be no known predisposing cause for these new lesions. They appear " out of the blue." They can, and do, occur when the patient is seemingly in the best physical condition. They are just as likely to occur during a sanatorium course as after it. Their appearance probably depends upon the balance between the patient's allergy and his immunity. There seems to be only one generalisation to be made about them, and that is that, if the patient is liable to them, they will tend to recur, and usually do so within a period of two years; though I have seen them after a free period of as long as ten years. But, as a general rule, if a patient, after treatment, does not have a relapse of this sort within two years, it is probable that he will remain free from them.

Clinical Evidence.—This depends to some extent on the size of the new lesion, but, unless very large, they give scanty and easily overlooked clinical evidence of their arrival. The usual picture is that of a mild influenzal attack with a short rise of temperature, seldom reaching 101°, and of only a few days' duration. The symptoms are usually those of general

malaise, and not such as to direct attention especially to the lungs. In severer cases there may be increase of sputum and cough, and perhaps, though rarely, hæmoptysis. With the very large new lesions the clinical picture in its early stages closely resembles lobar pneumonia.

Physical Signs.—Unless the lesion is large or is situated close to the lung surface, obvious physical signs are absent. When detectable, a patch suggesting broncho-pneumonia can be found—*i.e.*, dullness, altered breath sounds, and fine catarrh. Large lesions, or those situated close to the lung surface, give the physical signs of consolidated lung.

X-Ray Appearances.—The lesions appear as roughly circular, structureless, hazy shadows in previously clear portions of the lung-field. If watched by serial films they will be seen to shrink, lose their homogeneity, and either disappear or take on the usual stippled structure of the typical tubercular lesion.

Clinical Course.—In all but the gross lesions (and with these the condition is so obvious and urgent that I need not speak of them) all symptoms disappear entirely in ten to fourteen days or less, and the patient regains his *status quo ante*. This happens even though the new lesion is progressively enlarging. This period of immunity from symptoms varies, depending, probably, on the rate of spread of the new lesion, and may be anything from one to six months. It would seem to me that with such a spreading lesion the return of symptoms probably coincides with the erosion of a patent bronchus. The second group of symptoms, when they do appear, are the classical ones of pulmonary tuberculosis: cough, purulent sputum, perhaps hæmoptysis, malaise, weight loss, tachycardia, and fever. Physical signs, dependent on the size and location of the lesion, now make an obvious appearance, but it must be realised that by this time the new lesion is well-entrenched, much valuable time has been lost, and the chances of successful treatment diminished.

Recognition and Treatment.—It is vitally important to detect this type of relapse, if possible within a fortnight of its occurrence, and there is only one way to do so. That is to instruct the patient, who has finished his sanatorium course, to report at once if he has anything resembling an influenzal attack, or what is called a "feverish chill," and if he does so report, unnecessary though it may seem, an X-ray must be taken at once. The treatment, in spite of all protests, and ignoring any previous treatment, is to handle the patient as though he were a new, very early case. The original lesion will not influence the course of the new one and need not influence the general principles of its treatment. If caught quite early, these new lesions may disappear surprisingly surely and surprisingly quickly. But neglect of them spells disaster. A new lesion of this sort may be dealt with perhaps by two months or even less of complete rest under institutional

conditions, or even at home. If it is left until the second set of symptoms appear, it may mean months of sanatorium treatment, collapse, gold, etc., and even then the result may be unsatisfactory.

2.—Relapse due to the Direct Spread of a Temporarily Quiescent Lesion —"Spread Relapse."

Pathology and X-Ray.—The pathological picture is quite different in this type of relapse. In a typical case, a patient who has had a full course of hospital and sanatorium treatment has regained his health and returned to his normal home environment. He has lost his symptoms, or they have decreased and remain at their minimum. His X-rays films show that the lesions have contracted, become harder in outline, and there is no evidence of their spread or alteration in quality. In fact, the case is one of quiescent pulmonary tuberculosis in which the lesions, though potentially active and containing living bacilli, are static or even retrogressive, and there is a tendency to their conversion into fibrous scars or calcified nodules. If relapse of this type occurs, it will become obvious on serial X-ray examination that the lesions are losing their clean outline, tending to throw a denser shadow, and slowly but definitely invading the surrounding lung tissue. This is direct and visible evidence of reactivity of the tubercle bacilli and of definite spread by contiguity of the hitherto dormant fibro-caseous lesions.

Etiology.—It is obvious in such a case that, in spite of all evidence to the contrary, the lesions were not so soundly healed as they appeared to be and that the patient's present environment and habits are such as to lower his physiological tone and to allow of the reactivation of the tubercle bacilli which are always slumbering in such a lesion, however old. Since all the treatment of tuberculosis is governed by the method of trial and error, such a relapse might well be called the " insufficient-treatment " relapse, or the " wrong-environment " relapse.

Clinical Evidence.—What are the early symptoms of such a relapse? The answer is disconcerting—none, at first. I have seen such definitely spreading disease associated with steady weight gain, no reappearance of cough or sputum, and a level pulse and temperature chart. Careful analysis of patients' histories in relation to the extent and activity of their lesions when they come to diagnosis for the first time also assures us of the truth of this. If residual symptoms from the previous stage of activity have persisted, these may not alter, or do so so subtly that by their presence they tend to prevent the early recognition of such relapse. But it is no use being lulled into a false sense of security by this absence of symptoms. They will come surely enough in time, as in the previous type of relapse, and the quicker the spread the sooner they will appear. When they do arrive they are

again the classical ones of chronic pulmonary tuberculosis, and if action is delayed until they do appear, invaluable time will have been lost.

Physical Signs.—Physical examination can afford but belated evidence of this type of relapse. Comparatively gross spread will have taken place before a definite change in pre-existing signs can be detected. It is also obvious that the time of the appearance of new signs will depend upon the rate of spread, their character and intensity and upon the situation of the lesion.

Clinical Course.—As a rule, this type of spread is slow, and also, as a rule, if it is going to appear, it appears fairly soon after the sanatorium patient has returned to normal life. If it does not appear within one year or less after an apparently successful sanatorium course, unless the patient makes some radical change in his habits or environment (*e.g.*, complete change of residence, or work, or marriage), it should not occur at all. It must be borne in mind, however, that the spread may be very slow and gradual, and that unless a close look-out is kept for it, it may be missed and much and irreparable damage may be done before it gives clinical evidence of its presence.

Recognition and Treatment.—This type of relapse can only be detected by serial X-ray control. This should be the routine procedure for every case that has made a good response to treatment. The films must be taken at not more than three-month intervals—preferably more frequently at first—for two years at the very least. After that they can be with safety spaced to longer intervals. If the spread is detected soon after sanatorium treatment, it is probably wisest, if the patient's routine and environment are as good as they can be, to have recourse to further institutional treatment. But to save the expense and disappointment of this, if the spread is not a rapid one, a preliminary attempt may be made to check it by alteration of the patient's environment, habits, and routine under X-ray control. This will often be successful, for it may be said that this type of relapse is definitely indicative of a wrong mode of life for that individual patient. If, on the other hand, the spread is rapid and appears soon after the patient has had a full course of routine treatment, it is obvious that this alone is insufficient for his particular case, and collapse of the offending lung is probably indicated. These relapses are usually easy to recognise in the serial X-ray, but if there is not much difference between two successive films, careful comparison of the whole series side by side will usually make it obvious. Since, however, if it is not easily recognised, the spread must be very slow, not much damage can be done by waiting to make sure before seriously disturbing and uprooting your patient. This "wait and see" attitude, however, must be adopted with caution, and if definite evidence of continuous spread is obtained, action must be taken.

3. Relapses from Changes in a Previously Arrested Lesion with no Actual Spread of Disease Area—"Late Relapse."

This type may also be called the relapse of "late-cavitation" or the relapse of middle age.

Pathology and Etiology.—The so-called arrested lesion shows in the X-ray film as a dense, hard-outlined shadow, possibly containing calcified areas. We call it arrested because we can see it remain unaltered during a long period of time and producing no symptoms. But it is still capable of undergoing change and causing relapse. The lesions presumably consist mainly of fibrous tissue, but within the interstices of this there may be masses or nodules of encapsuled caseous material and certainly tubercle bacilli. The usual accident that occurs is the disturbance of the sleeping lesion, perhaps by actual physical strain, perhaps by the lowering of general immunity by intercurrent disease, more commonly by direct secondary pyogenic infection, and frequently by the normal lowering of general bodily vitality after middle life is passed. I have the impression that the commonest accident is for the lesion to become infected during an intercurrent pyogenic infection elsewhere in the respiratory tract. Tonsillitis, infected accessory sinuses, purulent naso-pharyngitis, pyorrhœa, and influenza are common culprits. The contents of the arrested lesion become inflamed, caseation increases, the liquid material points to the nearest patent bronchiole, is evacuated, and a cavity is formed. Or again, the patient may have been carrying a dry, symptomless cavity for years, when, either as a result of an intercurrent infection or because he has passed the zenith of his physiological life, insidious symptoms begin to appear.

X-Ray Evidence.—If the case has been under serial X-ray control, it will be seen that there is no actual spread of disease into fresh lung tissues. The area of the shadows remains unchanged or may even show contraction, but changes will be seen taking place within the shadowed area—changes usually indicative of cavitation. In the middle-age relapses, which are simply due to the infection of a previously clean cavity, no change may be seen at all in the X-ray picture.

Clinical Evidence and Symptoms.—The symptoms vary with the type of case. There is usually an insidious general deterioration of health, loss of weight, diminution of the usual vigour. Cough either appears or increases, sputum appears or increases and becomes more purulent, slight recurrent hæmoptysis unaccompanied by definite constitutional disturbance is common, and the middle-aged notice increasing dyspnœa. Recurrent "colds," "influenzas," "bronchial catarrhs," or "bronchitis," unrelated to weather conditions or epidemics, point to a perpetual source of infection somewhere in the respiratory tract. With the appearance of "late cavitation" of this

sort small calcareous lumps may be expectorated, and definite " late cavitation " is usually accompanied by an acute pyrexial attack and a sudden change in the character and quantity of the sputum and sometimes by hæmoptysis. The temperature, if recorded, will be found to be unstable between definite bouts of mild fever, and as time goes on all these symptoms tend to increase.

Treatment.—It must be remembered that in these cases we have to treat not progressive tuberculosis but rather an infected fibrocaseous and probably cavitated lung lesion caused by old tuberculosis. There is practically only one sure method of treatment and that is mechanical collapse. But before deciding on this, each case needs careful assessment, taking into consideration age, social and financial environment *vis-à-vis* health requirements, amount of incapacity from symptoms, and whether this incapacity is likely to increase. It must be appreciated, too, that a large number of patients with this type of relapse are at or over middle age, in whom collapse therapy must be approached with caution. The lesions are usually in the upper third of the lung, and the methods of collapse at our disposal are artificial pneumothorax, phrenicotomy, thoracoplasty, partial or complete, and apicolysis with paraffin plombage.

Artificial Pneumothorax.—This is a doubtful method in older patients. One does not care to induce an artificial pneumothorax in patients past middle age as a rule; it does not accord well with a rigid thorax and emphysema, though it has often been successfully done. Again, as the lesions are old-standing, that part of the lung in which they are situated is often firmly adherent to the parietal wall, thus preventing any useful collapse. In younger patients with a shorter history it is probably the best method of attack and should be the first to be considered.

Phrenicotomy.—This operation, with the relaxation of tension it brings to the whole lung and especially to its upper third, is often most efficacious in these cases. Age is no contraindication, the operation is simple, and it does not prevent more drastic treatment later if desired. At the worst, it leaves the condition unaltered. But it must be remembered that its beneficial results are often not apparent for three or four months.

Thoracoplasty, partial or complete, is called for if artificial pneumothorax fails and the symptoms are grave and increasing, and such as to threaten complete incapacity or even life itself. One must, however, be quite sure that the patient's age and general condition warrant it; but when life is threatened, risks are justified. It must be remembered, also, that an artificial pneumothorax is but a temporary collapse in most cases, and that with a grossly diseased lung the condition after re-expansion may be as bad or possibly worse than before. For this reason the desirability of a thoracoplasty in place of a pneumothorax should always be considered.

Apicolysis with Paraffin Plombage.—This should be the ideal treatment for localised apical lesions. I can quite believe that in the future it may be, but at present I cannot say that the average results I have seen have been any too successful. It is difficult to say why—perhaps the right operative technique has not yet been found. For myself, I would rather submit to a partial or complete thoracoplasty.

Non-Operative Treatment.—If collapse cannot be, or is not, used, the symptoms of this type of relapse can often be alleviated in many ways. Removal from an urban environment with its polluted atmosphere and frequent air-borne respiratory infections to a country life in a climate which suits the particular patient may sometimes almost effect a cure. Choosing the climate is difficult and can only be done by trial and error. I have known patients of this type who have flourished in the bracing air of Margate or Skegness and almost died at Torquay or Falmouth, and vice versa. Intercurrent respiratory infections are a great danger to them, wherefore they should be encouraged to live in sparsely populated districts and to shun the train, the shop, the cinema, the tea-party, and particularly the popular continental winter resorts whose central-heated hotels are hot-beds of this type of infection. If they are to winter abroad in search of dry air and sunshine, they should be able to afford to have their own house and to avoid infections as at home. The medium high plateaux of South Africa as a permanent residence are well worth consideration.

It is nearly always a hæmolytic streptococcus which is the offending secondary organism, and an autogenous vaccine, prepared from the sputum during a pyrexial attack, may be very valuable, not as a cure, but as a prophylactic against the recurrent pyrexial attacks and bronchitis to which these cases are so prone. Pyorrhœa alveolaris, so common in middle age, is a frequent cause or aggravator of this type of relapse. The mouth should be cautiously but conscientiously cleared if there is the slightest suspicion of dental sepsis. It is a good working rule that if more than half the number of existing teeth are septic, all should be removed.

Such cases should not be sent for sanatorium treatment. It is true they may derive temporary improvement from such treatment during the summer—largely due to the effect of purer air and the quiet routine life—but the sanatorium routine during the English winter is often definitely injurious, and sometimes fatal, to them. In any event it is time and money wasted, as the improvement, if any, is only temporary, and they leave the institution with exactly the same potentialities for ill-health with which they came. The non-operative treatment of such cases must be a *permanent* suitable alteration of environment and the control or, if possible, the eradication of obvious focal sepsis in the respiratory tract.

GENERAL ARTICLES

THE MANTOUX TEST: A COMPARISON OF OLD TUBERCULIN WITH TUBERCULIN PREPARED ON A SYNTHETIC PROTEIN-FREE MEDIUM*

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REFERENCE to recent literature shows that considerable lack of precision still exists with regard to certain aspects of the Mantoux test.

Long (1928), discussing the view that the tuberculin reaction is "less specific than is conventionally supposed," refers to the opinion of Selter (1926), based on experimental work, that bacterial infections of a variety of types sensitise the skin, not only to the specific germ of each infection, but to other bacterial proteins as well. He concludes: "In the last analysis it will probably be found that the specificity of the tuberculin reaction lies in its quantitative aspect. The significant fact is not so much that the tuberculous patient has a heightened sensitiveness to a variety of foreign, particularly bacterial proteins, as that he is extraordinarily sensitive to minute amounts of the active principle of tuberculin."

Non-specific reactions with tuberculin would thus arise: (1) As the result of a sensitiveness acquired from an infection other than tuberculous (*e.g.*, *B. coli*), or (2) from the (non-bacterial) protein of the broth in which the tuberculin is prepared acting on an individual sensitised to foreign protein, whether animal or not.

Fernbach and Herzger (1927) found that broth, or peptone water only, will give reactions in tuberculin-sensitive individuals, which generally disappear in 48 hours. Similar reactions could be obtained in tuberculin-negative persons by sensitising them with previous injections; they will afterwards react in the same way to definite quantities of dead tubercle bacilli as those tuberculin-positive. Later, these authors (1931) considerably elaborated this work. They found that tuberculous children could be distinguished as two groups: (*a*) *Purely (tuberculin) allergic children*, who do not react to a first injection of broth or peptone, but some react feebly after sensitisation by repeated injections. (*b*) *Tuberculin allergic para-allergic children*, who react strongly to a first injection of broth or peptone, or tend to develop a strong sensitivity. Moreover, in the purely allergic children intensification of an established tuberculin skin reaction will only occur as the result

* This investigation was carried out during the tenure of a Dorothy Temple Cross Research Fellowship in Tuberculosis awarded by the Medical Research Council.

of an injection of tuberculin, while in the second group it will also occur when peptone or broth is used, although a larger dose is required of the latter than of tuberculin. Finally, in tuberculin-negative (and therefore also peptone-negative) children sensitised to peptone, the skin reactions could also be intensified by the injection of either tuberculin or peptone, equal doses being needed, so that this intensification of a skin reaction is non-specific.*

Hart (1932, *a*) investigated, in both tuberculin-positive and -negative individuals, the reactions obtained by the intradermal injection of various dilutions of glycerine-veal-peptone broth similar to that used for the preparation of tuberculin. He found that "skin reactions qualitatively similar to the characteristic delayed response to tuberculin were elicited in a large number of individuals" (although more of the broth than the tuberculin was required), but that the incidence of skin sensitivity to the meat extract was practically identical with the incidence of tuberculin hypersensitiveness. Elsewhere, Hart (1932, *b*) therefore points out that controls with broth can be dispensed with in performing the Mantoux test. Nevertheless he considers it "desirable to use them when performing tests with 1 : 10 tuberculin or stronger solutions, in order to avoid confusion between true tuberculin reactions and the delayed, atypical, non-specific reactions which follow with comparative frequency the injection of these concentrated solutions"—presumably in non-infected individuals sensitised by the injection of the weaker solutions.

Ustvedt (1932) states that "it must be admitted that . . . one obtains sometimes, in subjects giving a negative tuberculin test, reactions which are scarcely distinguishable from true tuberculin reactions." He suggests the size of the positive Mantoux reaction is made up of a specific and a non-specific part. He tested 53 patients† intradermally with 1 mg. of broth (in 0·1 c.c. saline) and obtained infiltration and erythema 10 mm. or more in diameter in 7 after 48 hours; in 2 patients the reaction remained unaltered at 72 hours. By concentration of the broth, the frequency and intensity of the reactions increased.

Söderling (1934) considers that non-specific reactions due to the broth occur in tuberculin-positive individuals only, and that these can generally be distinguished from specific reactions; for instance, induration is often present without erythema. The reactions are more marked the more concentrated the broth, when they are sometimes indistinguishable from true tuberculin reactions.

Consideration of the work of the authors quoted leads to the conclusion that caution must be observed in the interpretation of feeble Mantoux reactions, and of those obtained with strong solutions of tuberculin.‡ There exists at present no unanimity as to the criteria on which a reaction is to be interpreted as definitely positive. The limits of a few authors may be cited in illustration: Cummins and Walker (1931), 2 mm. erythema; Hart (1932, *b*), erythema or erythematous infiltration 5 mm. in diameter; Bergman (1932), erythema 5 mm. in diameter with infiltration; Opie and McPhedran (1926), Wallgren (1928), Ustvedt (1932), and Söderling (1934), 10 mm. erythema with infiltration. Moreover, some workers alter the criteria with the dilution employed. Thus Arborelius (1932) requires 10 mm. erythema with infiltration when 1 in 1,000 tuberculin is injected,

* This conclusion is of great importance in view of the results published by Debré, Lelong, and Pictet (1932), claiming over 95 per cent. of positive Mantoux tests in children vaccinated orally with B.C.G. Many of these positive reactions consisted merely of staining showing only after several injections of increasing concentrations of tuberculin up to 1 cgm.; no control of broth was used.

† It is not stated whether they were tuberculin-positive or -negative.

‡ It should be emphasised that the injection of broth, even in concentration equal to that in the tuberculin, does not serve as an accurate control, as the composition of the "broth part" in the tuberculin is probably altered as the result of the growth of the tubercle bacilli.

but is satisfied with a 5 mm. papule when the 1 in 100 solution is employed. Debré, Lelong, and Pictet (1932) state: "Toutes les réactions franchment positives se ressemblent. Seul leur diamètre et l'induration diminuent un peu au fur et à mesure que l'on doit augmenter la dose de tuberculine pour les provoquer." (No measurements are given.) In view of the work quoted above, showing the sensitisation to broth, it would seem more logical to demand an increase, rather than a decrease, in the size of a positive reaction when the test is repeated with a stronger solution.

It should also be noted that there is no general agreement as to whether the reading of the test should be taken at 48 or 72 hours.

By repeating the test with a stronger solution of tuberculin when reactions showing erythema about 5 to 9 mm. in diameter were obtained at 48 hours, the writer has shown (1934) that a certain proportion of these "doubtful" or "feeble" reactions are not specific, and that therefore 10 mm. erythema with infiltration is a safer definition of a positive reaction, particularly for practitioners who have not the experience obtained in performing a large number of tests.

v. Gröer (1934) has suggested an original conception of allergy which he believes fits in much better with the varying clinical course of tuberculosis. According to him, the tuberculin reaction is the result of the interaction of two factors: *Empfindlichkeit* (S = *susceptibilitas*), and *Reaktionsfähigkeit* (R). S represents the increased sensitiveness of the tissues to the tubercle toxin—*i.e.*, the capacity to be injured by the virus; R, on the other hand, is the power to react to the injury. These two properties, altered by every dose of toxin admitted to the circulation, usually, but not necessarily, run hand in hand. By performing intracutaneous tests in tuberculin-positive children simultaneously with dilutions of tuberculin ranging from 1 in 10^9 to 1 in 100, he and v. Chwalibogowski (1934) have shown that while the size of reactions obtained usually bears a direct relation to the concentration of tuberculin used, this is not always the case, and that two other groups of children can be distinguished. In the first the reactions with the weaker dilutions are much bigger than one would expect mathematically (thus in some cases there was almost no difference between 1 in 10,000 and 1 in 1,000,000)—*i.e.*, $S > R$; the tissues are so sensitive that a very small dose of tuberculin produces almost the full response possible. In the second group, on the other hand, the size of reaction with the weaker solutions is much smaller than one would expect mathematically—*i.e.*, $R > S$; a very big dose of tuberculin is required to stimulate the sensitiveness, which is relatively low. It will be seen that, according to this conception, it may be fallacious to assume that a "feeble" reaction is non-specific because a concentration ten times stronger gives a reaction no greater. But clearly the subject requires further investigation, particularly as the authors, for purpose of comparison, assumed the response to each injection to be the maximal erythema obtained from 36 hours onwards, thus most probably including the non-specific response.

In supporting the fixing of a 10 mm. erythema and infiltration limit at 48 hours for a positive Mantoux reaction, the writer does not wish to imply that such a criterion will exclude with certainty non-specific reactions, or that a reaction of smaller extent cannot represent a specific response. Reactions of 5 mm. or over include three types: (1) Feebly positive specific reactions (becoming definitely positive with a stronger solution of tuberculin); (2) the early stage of a delayed positive specific reaction (developing to definitely

positive after 72 or 96 hours); and (3) non-specific reactions due to the peptone in the broth.

The possibility of obtaining tuberculin by growing the bacilli on a synthetic protein-free medium appears theoretically to solve the difficulty associated with the occurrence of the non-specific reactions. Long and Seibert (1926) showed, however, that in such a medium tuberculin activity developed coincidently with the appearance of protein in the medium, being derived presumably by extraction or autolysis of the tubercle bacilli. Nevertheless it would be of practical interest to compare the results obtained with the two types of tuberculin.

Hart (1932, *a*) carried out the intradermal test with a tuberculin (S.T.) prepared on a protein-free medium, the latter having given negative results when tested for skin sensitivity on patients with manifest tuberculosis. He found that every individual reacting to old tuberculin (O.T.) gave typical positive reactions also to S.T., although stronger solutions were sometimes required. The tests were carried out, however, merely to show that it was not the broth of the O.T. which was responsible for the reactions obtained in tubercle-infected individuals with O.T. Hence no details of relative size are given, nor is it stated whether the S.T. was previously standardised; and, finally, no tests were carried out on individuals negative to O.T.

The following preliminary investigation was carried out with the object of obtaining some indication as to whether the use of a tuberculin prepared on a synthetic protein-free medium (S.T.) would facilitate the reading of feeble tuberculin reactions:

Material and Technique of Investigation.

One hundred and fourteen children and adults, out-patients attending the Central Tuberculosis Dispensary at Barcelona, were tested with both O.T. and S.T. Sixteen were diagnosed as clinical tuberculosis; the remainder consisted chiefly of B.C.G. vaccinated children and home-contacts attending for routine examination. While the endeavour was made to see each patient at least 24 and 48 hours after each test, this was not always possible. One hundred and eleven patients were tested with 1 in 1,000 dilution. Of the 61 doubtful or negative with this dilution at 48 hours, 37 were tested with 1 in 100 (and two more who had not previously been tested with 1 in 1,000). Of the 36 doubtful or negative with 1 in 100, 32 were tested with the tuberculin 1 in 10. The number of patients seen at 24 and/or 48 hours after the injection of each dilution is indicated in the tables.

Commercial Koch's O.T., standardised at Frankfurt a/M., and therefore by the "shock" method, was employed. This tuberculin usually produces a skin reaction (visible on fourth day) in an infected guinea-pig in a dose of 0·001 mgm. (P. Domingo). The S.T. was prepared from a 45-day culture on Sauton's medium.* After heating for 30 minutes at 115° C. it was evaporated to a tenth of its bulk, filtered, and then titrated by the method of Lexis and Aronson. Guinea-pigs infected 3 weeks previously with 0·1 mgm. of bovine tubercle bacilli gave a positive skin reaction (4 days) with 0·006 gm. tuberculin intradermally. Dilutions were prepared weekly with normal saline and 0·5 per cent. phenol. When the dilutions 1 in 10 were employed, controls of glycerine-veal-peptone broth (concentrated to a tenth of bulk and then diluted ten times) and of unaltered Sauton's medium were injected at the same time.

* The composition is as follows: Asparagine 4 gm., pure glycerine 60 gm., citric acid 2 gm., acid potassium phosphate 0·5 gm., magnesium sulphate 0·5 gm., ammon. citrate deferv. 0·05 gm., water 940 gm.

Separate syringes and needles clearly labelled were used *and kept* for each dilution, tuberculin, and controls. The O.T. was always injected on the right and the S.T. on the left forearm. Tests, doubtful or negative at 48 (or 72) hours with 1 in 1,000, performed on the upper part, were repeated with 1 in 100 on the middle of the forearm. The 1 in 10 dilutions were similarly employed 2 or 3 days later on the lower part of the forearm, the control fluid being injected at the side of the tuberculin. 0·1 c.c. was the dose each time.

All reactions, however slight, were measured in both diameters and the degree of erythema and infiltration, as well as bruising, noted.

A positive reaction was constituted by an area of erythema 10 mm. in diameter with infiltration obtained with the O.T. at 48 hours.

Results.

The size of the reaction was estimated by multiplying the two diameters of the erythema. In this way an area of erythema greater than in actual fact was obtained, as it generally adopts the form of a circle or ellipse. For the purpose of comparing the two tuberculins this discrepancy is of no importance and the method used considerably facilitates calculation. It was considered advisable to discount small differences due to experimental error in measurements, volume injected, and depth of skin at which the needle is introduced. Hence S.T. reactions less than 25 per cent. smaller or greater than the O.T. were assumed to be equal.* Thus, 10×10 mm. (=100 sq. mm.) O.T. and 6×12 mm. (=72 sq. mm.) S.T. would be considered as O.T.>S.T., but if the S.T. were 8×10 mm. (=80 sq. mm.), the reaction would be classified as O.T.=S.T.

The results obtained with the three dilutions are shown in the following tables:

TABLE I.

DILUTIONS 1 IN 1,000.

111 patients tested: (*a*) 72 seen at 24 hours, and 48 or 72 hours; (*b*) 17 seen at 24 hours only; (*c*) 22 seen at 48 or 72 hours only.

A. Of (*a*) and (*c*)—*i.e.*, 94 patients—50 were positive (*i.e.*, showed with O.T. at least erythema 10×10 mm. with infiltration). These 50 reactions can be classified as follows (size at 48 hours):

O.T.>S.T.: 34 (68 per cent.).†
(20 [40 per cent.] were twice as much in area.)
O.T.=S.T.: 10 (20 per cent.).
S.T.>O.T.: 6 (12 per cent.).

B. There were no non-specific positive reactions—*i.e.*, there was no erythema 10×10 mm. at 24 hours, which became smaller at 48 hours.

* It may be added, in view of the results to be quoted, that as regards these small differences the O.T.>S.T. reactions considerably preponderated.

† 8 of these were under 10×10 mm., but above 5×5 mm. in size, only 1 case of clinical tuberculosis being included in these.

39 of the positive reactions (indicated in A) were seen at 24 hours, and at 48 or 72 hours. The relative areas were:

At 24 Hours.		*At 48 or 72 Hours.*
24 (61 per cent.)	O.T.>S.T.	27 (69 per cent.)
19 (48 per cent.)	(twice as much in area)	17 (43 per cent.)
8 (20 per cent.)	O.T.=S.T.	7 (18 per cent.)
7 (18 per cent.)	S.T.>O.T.	5 (12 per cent.)

C. In the 72 tests seen at 24 hours and later—

At 24 hours there were 8 reactions 5×5 mm. to 9×10 mm. with O.T.; only one of these was as big as 5×5 mm. with S.T.

At 48 hours there were 5 reactions 5×5 mm. to 9×10 mm. with O.T. (*all no greater with the dilution* 1 *in* 100), but the corresponding S.T. tests were all less than 5×5 mm.

D. The number of minimal reactions (*i.e.*, under 5×5 mm.) were (at 48 hours) 21 with O.T. and 16 with S.T.

TABLE II.

Dilutions 1 in 100.

39 patients tested: 14 were seen at 24 hours, and 48 or 72 hours; 10 were seen at 24 hours only; 15 were seen at 48 hours only.

A. There were 3 positives: 1 (O.T.=S.T.) which had not been tested with 1 in 1,000, 2 (O.T. twice S.T.) who had already been only just positive with 1 in 1,000. Of these 3 positives, 2 were seen at 24 hours as well; in 1 both O.T. and S.T. were over 10×10 mm., in the other O.T. was over 10×10 mm. and S.T. less than 5×5 mm.

B. There was 1 non-specific positive reaction with O.T. at 24 hours—*i.e.*, it was over 10×10 mm. (less than 5×5 mm. with S.T.) at 24 hours and less than 5×5 mm. at 48 hours.

C. Both at 24 hours and at 48 hours there were 7 doubtful (*i.e.*, 5×5 mm. to 9×10 mm.) reactions with O.T. (4 no greater with 1 in 10, 1 over 10×10 mm. with 1 in 10 and no infiltration, 2 not retested)—all these were under 5×5 mm. with S.T. In addition there was 1 reaction (5×5 to 9×10 mm.) with S.T. both at 24 and 48 hours, being less with O.T: 1° 5×6 mm. at 24 hours, 2×2 mm. at 48 hours, no greater with 1 in 10; 2° 7×9 mm. at 48 hours, less with 1 in 10.

D. There were 7 minimal reactions with O.T. and 9 with S.T.

TABLE III.

Dilutions 1 in 10.

32 patients tested (of these, 1 with O.T. only and 1 with S.T. only): 20 were seen at 24 and 48 hours; 6 were seen at 24 hours only; 6 were seen at 48 hours only.

The results with the tuberculins and controls were as follows:

Size.	*O.T.*	*Broth Control (22 Patients Only).*	*S.T.*	*Sauton Control (31 Patients Only).*
At 24 hours :				
10×10 mm.	6	2	2	—
5×5 mm.	6	3	5	—
Less	11	7	16	17
At 48 hours :				
10×10 mm.	2*	—	—	—
5×5 mm.	—	—	1	7
Less	11	4	10	

Discussion.

Examination of the tables suggests the following points for consideration:

(1) At 48 hours about 70 per cent. of the positive O.T. reactions are definitely greater (in 40 per cent. twice as big) as the S.T. reactions. This may be due to one or both of the following factors: (*a*) the difference in strength of the two tuberculins, and (*b*) the absence with S.T. of the non-specific reaction due to the broth peptone of the O.T. It is probable that the larger difference can be accounted for by (*a*) alone, as by the intradermal test on guinea-pigs the O.T. is six times the strength of the S.T. If (*b*) played an important rôle, one would expect the percentages of O.T.>S.T. reactions to be greater at 24 hours (when non-specific reactions are most marked) than at 48 hours. Table I., B, shows, however, that this is not so. That non-specific reactions may also occur with S.T. in stronger solutions is shown, moreover, by the finding of the following:

1 in 100 S.T.: One reaction 7×9 mm. at 48 hours; repetition of the test with 1 in 10 solution showed the above reaction to be non-specific.

1 in 10 S.T.: Two reactions 10 mm. and five reactions over 5 mm. in diameter at 24 hours; all disappeared at 48 hours.

The appearance of these non-specific reactions is easily explained if it is admitted that the protein produced from the tubercle bacilli in the synthetic medium may have a non-specific as well as a specific effect.

* The erythema was very faint and there was no infiltration. It is very doubtful whether these reactions should be assumed as specific positive. It is of interest that they occurred in B.C.G vaccinated children.

(2) Nevertheless, in non-tuberculous individuals, S.T. gives rise to less non-specific reactions than O.T. All the O.T. reactions 5 to 9 mm. at 48 hours, which did not prove to be positive by a stronger injection, were associated with negative (*i.e.*, under 5 mm.) S.T. reactions. This difference cannot be due to the different strength of the tuberculins, since injections of ten times the strength of the S.T. did not result in a positive reaction.

(3) It is tentatively suggested that the rapidly subsiding non-specific reactions are due to a non-specific action of the protein derived from the tubercle bacilli, and the more lasting non-specific reactions are the result of the increased proportion of protein in the O.T. from the broth. This increased protein is clearly of importance in sensitising the skin to later injections.

(4) The limits for a positive reaction with S.T. are definitely lower than with O.T. Thus amongst the S.T. reactions (at 48 hours) corresponding to the positive O.T. reactions, 8 were between 5 and 9 mm. in diameter. It has been suggested that S.T., owing to its weaker strength, might be used in a stronger concentration than O.T. for the first test, thus minimising the number of injections required for the complete Mantoux test. The present investigation definitely shows that this would not be safe, as reactions of the following sizes were obtained with the S.T. 1 in 1,000: 28×34, 30×40, 42×77, and 50×60 mm., the last two in cases of clinical tuberculosis.

(5) The equal number of minimal reactions (*i.e.*, under 5 mm.) obtained with the two tuberculins, and even with Sauton's medium only, indicates that these are due to "trauma" or some common chemical constituent (? glycerine). It is of interest to note that Ekberg, Malmros, and Roos (1934) tested 63 new-born infants with tuberculin. After injection of 1 mg. (*i.e.*, 1 in 100 dilution) "a very slight reaction was obtained in a few cases, but in no case did it exceed 3×3 mm."

(6) It appears that, in practice, the use of a standardised* S.T. would offer advantages in excluding delayed non-specific reactions, especially when strong concentrations of tuberculin are used. The question of the stability of the S.T. will also have to be considered, as it has been suggested (Hart, 1932, *b*) that it is not as stable in dilution. In a recent paper Douglas and Hartley (1934) state that there is no evidence to show that dilutions of O.T. prepared by the use of synthetic media are any less stable than similar dilutions of the International Standard O.T.

* The method to be employed here would have to be carefully considered in view of the work of Küster and Pockel (1933), not yet confirmed, who found that a dialysed Sauton tuberculin which will produce a positive intradermal test in a guinea-pig in the same strength as O.T. has nevertheless to be used in a dose 100 times that of O.T. to cause the death of the guinea-pig. This suggests that the toxic property and the skin reaction property may be associated with different chemical substances in the tuberculin.

Summary.

Evidence from the literature is brought forward indicating the need for caution in interpreting feeble reactions (especially if strong solutions of tuberculin are employed) when carrying out the Mantoux test, in view of the occurrence of non-specific protein reactions. An investigation is described in which the Mantoux test was carried out both with Old Tuberculin (O.T.) and tuberculin prepared on a synthetic protein-free medium (S.T.). It is suggested that the use of a tuberculin prepared on a protein-free medium may offer advantages in excluding non-specific delayed reactions.

I am greatly indebted to Professor P. Domingo, who suggested the investigation and supplied the tuberculins and control solutions; to Professor L. Sayé, who offered me the fullest facilities for carrying out the work at his dispensary; and to Dr. J. Domenech Alsina for much valuable assistance.

Addendum.

Since the above was written the writer has seen a paper by M. Dorset (" A Comparison of Koch's Old Tuberculin with a New Synthetic Medium Tuberculin "), read at the Annual Meeting of the United States Live Stock Sanitary Association in December, 1933. This paper (and subsequent discussion) appear in the *J. Am. Vet. M. A.*, 1934, N.S., xxxvii. 439. The synthetic medium used differed slightly in composition from that described in this paper. The tuberculin obtained from it (? what day culture used) proved to be two to four times as potent as the O.T. as standardised by the " shock " method—*i.e.*, the power to kill tuberculous guinea-pigs. (This method is widely recognised as not sufficiently reliable to detect even wide difference in potency. See report on tuberculin standardisation, the work of the Serum Institute, Copenhagen, published by the Health Section of the League of Nations, in the press.) As a result of comparative tests on animals, Dorset came to the conclusion that the tuberculin obtained by growth on a synthetic medium was more reliable than the O.T. In connection with the discussion in the writer's paper it is of special interest to give here the composition of the Dorset filtrates from cultures grown on broth and synthetic media.

	Culture on Broth Medium (Per Cent.).	*Cultures on Synthetic Medium (Per Cent.).*
Ash	0·85	0·15
Protein	1·40	0·32
Carbohydrates	None	0·30
Glycerin	3·34	0·04
Total solids	5·59	0·81

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THE EXAMINATION OF BLOOD BY LOEWENSTEIN'S METHOD FOR THE PRESENCE OF B. TUBERCULOSIS

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IN 1931, being interested in the distribution of *B. tuberculosis* in the organs of heavily infected cattle, I attempted to demonstrate the presence of this organism in the blood stream of these animals. The method used was Loewenstein's acetic-acid, sulphuric-acid technique (Loewenstein, 1930). The bloods from fifteen tuberculous cattle, mostly cows, and all heavily infected, were examined, and no positive result was obtained.

At the same time my colleague, Dr. D. Brown (unpublished results), applied the same method in the examination of 20 cases of definitely proved human tuberculosis, and again with negative results.

I communicated the unsatisfactory nature of our investigations to Professor Loewenstein, and he suggested that probably it was due to some error

in technique. At that time, being unable to visit Vienna and learn the proper technique, the investigation was discontinued; but in 1933 I was fortunate to receive a visit from Herr G. Loewenstein, who kindly demonstrated his father's more recent technique (Loewenstein, 1933). Since then I have examined 30 cases of progressive pulmonary tuberculosis (third stage), 10 cases of lupus, and 4 cases of erythema multiforme in man, and 10 cases of very advanced generalised tuberculosis in bovines.

No positive results were obtained.

As Loewenstein has modified this technique on many occasions, as some of the description of these techniques is somewhat vague, and as, according to him, success is only to be obtained after careful attention even to the most minute detail, it appears advisable to give a detailed description of the method employed.

Preparation of Medium.—Five fresh eggs were cleaned by immersion for half an hour in a solution of 5 per cent. green soap and 5 per cent. sodium bicarbonate in distilled water. During this treatment the shells were thoroughly scrubbed. They were next washed in distilled water and soaked for twenty minutes in a 1 in 1,000 solution of corrosive sublimate in distilled water. Finally, they were washed in running sterile distilled water. In handling the eggs after immersion in the corrosive sublimate solution a strictly aseptic technique was employed. (Sterile rubber gloves which had been thoroughly washed in distilled water before sterilisation were used. No powder was employed.) The distilled water was always freshly prepared and sterilised immediately after distillation.

A scrupulously clean glass distillation apparatus was used.

The following solutions were prepared and sterilised:

Asparagine Solution.—This consisted of:

Asparagine (Merck)	3·0 grm.
Di-potassium phosphate (Merck) (K_2HPO_4) ...	1·0 grm.
Tribasic sodium citrate (Kahlbaum)	1·0 grm.
Magnesium sulphate (pure crystalline) (Kahlbaum)	1·0 grm.
Glycerol (31° Bé.) (Kahlbaum)	60·0 c.c.
Distilled water	1,000·0 c.c.

This was sterilised in steam for two hours.

Congo Red Solution.—This consisted of 2 per cent. congo red (Grübler, Leipzig) in distilled water and was sterilised by autoclaving at 15 pounds pressure for twenty minutes.

Malachite Green Solution.—This consisted of 2 per cent. malachite green (Grübler, Leipzig) in distilled water and was sterilised in steam for two hours.

Congo Red Medium.—This was prepared as follows: 150 c.c. of the asparagine solution, 6 grm. of potato starch (free from acid-fast organisms), and

12 c.c. of glycerol were placed in a sterile flask of 500 c.c. capacity containing sterile glass beads. After thorough mixing this was sterilised in steam for two hours, and when cooled to about 55° C. the contents of four eggs and the yolk of another were added. This was thoroughly shaken, the cotton-wool plug having been replaced by a sterile rubber bung; 5 c.c. of the sterile congo red solution were then added and the mixture was again well shaken. The medium was next filtered with strict aseptic precautions through four layers of sterile gauze into a sterile flask. It was now tubed into sterile 6-inch by $\frac{5}{8}$-inch test tubes plugged with cotton-wool; 5 c.c. of the medium were introduced into each tube.

The tubes were sterilised in the sloped position in an inspissator for two hours at 80° C. on two successive days. They were then kept in the dark and always used before the tenth day after preparation. Sterility was controlled by placing them in the incubator at 37° C. for two days.

Malachite Green Medium.—This was prepared in the same way as has just been described for the congo red medium, except that 5 c.c. of the malachite green solution were added in place of the congo red solution.

Method of preparing the Inoculum from the Blood.—The blood was obtained from the median basilic vein in the human cases and from the external jugular vein in cattle. In the latter the blood was collected when they were slaughtered. The animal was shot with the captive bolt pistol, and immediately it fell the skin over the jugular furrow was slit and the external jugular vein exposed. The blood was then withdrawn with aseptic precautions. In every case, both human and bovine, the blood was collected in a 30 c.c. Behring venule containing 5 c.c. of a 3·8 per cent. sterile aqueous solution of sodium citrate. The venule was thoroughly shaken immediately the blood was withdrawn to prevent clotting. The amount of blood used was never less than 20 c.c. and never more than 24 c.c. The citrated blood was thoroughly mixed in a sterile centrifuge tube of 150 c.c. capacity with 80 c.c. of sterile distilled water, and after the red blood corpuscles had lysed it was centrifugalised. (In all cases where centrifugalisation is mentioned it is to be understood that it means for twenty minutes at 2,000 revolutions per minute.) The supernatant fluid was discarded and the deposit again thoroughly mixed with another 80 c.c. of sterile distilled water. This was centrifugalised and the deposit was generally of a greyish colour and free from hæmoglobin. If not, it was subjected to another such treatment. In mixing the various deposits with distilled water it was occasionally difficult to get them thoroughly dispersed. In such cases the distilled water was added in small amounts at a time and the deposits thoroughly broken up and mixed with a sterile glass rod. To the hæmoglobin-free deposit 2 c.c. of a 15 per cent. aqueous solution of sulphuric acid were added,

and the deposit was quickly but thoroughtly broken up, if necessary with the aid of a sterile glass rod.

The sulphuric acid was allowed to act for exactly three minutes. At the end of this period 80 c.c. of sterile distilled water were quickly added, and the mixture was centrifugalised. The deposit was again washed with another 80 c.c. of sterile distilled water to get rid of any remaining trace of acid, and after resuspension in about 2 c.c. of sterile saline (0·85 per cent. NaCl) was ready for inoculation.

Method of Inoculation of Tubes.—These culture tubes were inoculated either on the day the blood was obtained or on the following day. Four tubes—viz., two congo red and two malachite green slopes—were inoculated in each examination. A wide-bore 1 c.c. pipette was used, and about 0·5 c.c. of the inoculum was introduced into each tube. The whole surface of the medium was covered, care being taken not to break the surface. The superfluous cotton-wool of the plugs was cut off and the tubes carefully sealed with sealing wax. A good deal of trouble was taken to ensure that during the first twenty-four hours, when the tubes were kept in the sloped position, the inoculum was evenly distributed over the surface of the medium. After this the tubes were incubated in the vertical position at 37° C. and kept in the dark.

These preparations were examined for macroscopic growth at weekly intervals, and at the end of six weeks, no growth being observable, the surface was scraped with a platinum loop and films made. These were stained by Ziehl-Neelsen's method and decolorised with acid and alcohol. As no acid- and alcohol-fast bacilli were detected the tubes were resealed and incubated for a further six weeks. Films were again made and stained as above described, and again the results were negative. Two c.c. of sterile saline (0·85 per cent. NaCl) were added to each tube, and the surface of the medium was thoroughly rubbed over with a sterile throat swab. The suspension from a congo red slope was added to that from a malachite green slope and then inoculated subcutaneously into the groin of a guinea-pig. Another guinea-pig received a similar inoculation from the remaining two slopes, except when the blood was obtained from lupus cases, and then the suspension was inoculated subcutaneously into the right pectoral region of a fowl. All the fowls and guinea-pigs were killed at the end of three months, and none showed any signs of tuberculosis. In 4 cases one of the duplicate guinea-pigs died from intercurrent infection.

Before inoculation of the tubes a little of the original inoculum obtained from each blood was spread on slides and stained by Ziehl-Neelsen's method with acid and alcohol decolorisation. No alcohol- and acid-fast bacilli were seen.

Discussion.

It is not intended to give a complete bibliography. This can be obtained in a Medical Research Council's publication (Wilson, 1933) and in two papers by Kallós and Kallós-Deffner (1932, 1934). To give an idea of the tremendous amount of work carried out in the investigation of tuberculous bacillæmia, there are 148 references in Kallós and Kallós-Deffner's first paper and 130 in their second. Their first deals with papers published between 1910 and 1932, whilst the second is concerned with papers appearing between 1932 and 1934. For the second half of 1934 there are at least twenty-one publications dealing with Loewenstein's method alone.

The results of these investigations are most contradictory. For instance, Loewenstein obtained positive results in 80 to 100 per cent. of cases of progressive pulmonary tuberculosis (third stage) (Loewenstein and Russeff, 1930; Loewenstein, 1931), whilst Maier (1934) did not get any positive results in 198 cases of a similar nature.

In skin tuberculosis, Kren and Loewenstein (1931) got 62 per cent. positive blood cultures, whilst Holm (1932) had not a positive result in the examination of 90 such cases.

Indeed, in addition to the above, Loewenstein and his colleagues have obtained quite high percentages of positive blood cultures in practically all forms of tuberculosis, and even in such conditions as chorea, acute polyarthritis, rheumatic endocarditis, dementia præcox, multiple sclerosis, retrobulbar neuritis, polycythæmia rubra and teno-synovitis.

Kolle and Küster (1934) examined 885 patients suffering from conditions similar to those in which Loewenstein had obtained numerous positive results. They used Loewenstein's technique, and got only 7 positive results.

Though I have been totally unsuccessful in repeating Loewenstein's work, I must, in fairness to him, state that he sent me six cultures obtained from the blood of the following cases—viz., 2 from skin tuberculosis, 2 from polyarthritis, 1 from lupus, and 1 from tuberculosis of the knee-joint. All these cultures were indubitably pure growths of *B. tuberculosis*.

Griffith (1933) examined 27 cultures sent to him by Loewenstein and found that all were cultures of *B. tuberculosis*, 17 being of the human type and 7 of the avian.

Loewenstein has stressed the importance of his so-called "micro-cultures." He scrapes the surface of his cultures after six weeks' incubation, even though there is no visible growth, and examines the material so obtained for the presence of acid-fast organisms.

He and his colleagues have obtained many positive results, but have usually been unable either to subculture from these positive micro-

cultures or to produce tuberculosis in guinea-pigs by inoculation of the scrapings.

Many possible fallacies have been indicated.

1. Eichbaum (1932*a*) and others have demonstrated the frequent presence of acid-fast bacilli on the interior of water taps.

2. Many authors have pointed out the danger of mistaking portions of red blood corpuscles and leucocytes as well as other artefacts for tubercle bacilli. These may appear acid-fast, and may closely resemble that organism.

3. Over-fixation of films containing relatively large amounts of organic material may cause difficulty in decolorisation (Coveney and Edington, 1934).

4. Acid-fast bacilli have been isolated from the skin covering the flexures of the elbow and the knee (Eichbaum, 1932*b*) and from comedones (Schwabacher, 1933).

5. That acid-fast bacilli may be present in dust is well known ; therefore any method—*e.g.*, the one under discussion—which is liable to aerial contamination may be vitiated by the introduction of such organisms.

6. It has been suggested that the eggs from which the medium is made may contain tubercle bacilli of the avian type. Only about 1 per cent. of the eggs from tuberculous hens contains tubercle bacilli (Fitch and Lubbenhusen, 1928).

7. Non-pathogenic acid-fast bacilli have on many occasions been isolated from the blood stream of both healthy and diseased animals and men (Schwabacher, 1933).

I have found that certain batches of potato starch are contaminated with acid-fast bacilli. Considering the method of manufacture of such starch, this is by no means surprising. In connection with this it is worth noting that there are many types of actinomyces present in the soil, and that some of these are causal of potato scab. Further, the filaments of some of these actinomyces, particularly the aerial hyphæ, are acid-fast, and as there is a tendency for them to fragment they may give the impression that they are acid-fast bacilli. The resistance of some of these acid-fast organisms obtained from starch to acid and even to acid and alcohol decolorisation is greatly increased if the organism is grown in a fluid egg medium.

In staining direct film preparations from a medium containing potato starch, portions of the starch granules may retain the stain after acid decolorisation, and thus closely resemble *B. tuberculosis*.

From the above one can well imagine that Loewenstein's micro-cultures have not met with universal approval.

Conclusion.

The position at present is that those who are unsuccessful damn the method with faint praise, whilst those who are successful explain the negative results of their less fortunate colleagues as due to faulty technique.

I wish to tender my thanks and appreciation of their help to Professor Loewenstein and to his son Herr G. Loewenstein. I also thank Dr. D. Brown for permission to publish the results of her investigations, Dr. R. Hallam for the specimens of blood from cases of lupus and erythema multiforme, and Dr. Doig for those from the cases of pulmonary tuberculosis.

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THE ARRESTED CASE OF TUBERCULOSIS IN THE VILLAGE SETTLEMENT

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IN the report on Preston Hall for the year ending September, 1933, I ventured to launch the criticism that the Village Settlement for the tuberculous must henceforth take into consideration more than has been the custom in the past the clinical features in individual cases resident in the village. I suggested that it was not the function of the Village Settlement to provide security of tenure in employment for ex-patients for indeterminate periods, irrespective of their physical condition, but that the essential object was to

bring active disease to a state of arrest over a period sufficiently long to reduce the liability of relapse to a minimum.

If the purely medical considerations are not to be the basis of the Village Settlement, then the results, however valuable they may appear on the economic side, must always be open to criticism by a discerning medical public.

Since the publication of the report already referred to I have, quite naturally, been questioned on the wisdom of this new line of thought by a few; on the other hand, I have the evidence of many of my colleagues in the tuberculosis service that this new policy, with all its implications, has at last placed the Village Settlement in its proper sphere as a residential centre for the genuinely tuberculous.

On September 30, 1933, there were no fewer than fifty-six men living in the village at Preston Hall who were, in our opinion, arrested cases of tuberculosis. What was to be the future of such cases? Without exception these men had been in the settlement for five years or more, and had not been subject to relapse during the five years preceding September, 1933. Some had, in fact, shown no signs of active disease for a period of ten consecutive years. Of this we are again certain, that the great majority of these men will ultimately die of diseases other than tuberculosis. Unless the Village Settlement makes some provision for the substitution of these cases, then the major object for which the settlement exists—the treatment of tuberculosis—will be to a large extent unfulfilled.

There is no justification whatever for keeping a man who has had arrested disease for five consecutive years in continued residence under the sheltered conditions appertaining in the Village Settlement, more especially if he is not a key-man in any of the departments. He has no real claim to be given all the medical advantages which are so necessary for the man who is subject to relapse. I take the view that the arrested case should no longer be a stumbling-block to the medical progress of so valuable an instrument in the treatment of tuberculosis as the Village Settlement.

A detailed analysis of the fifty-six cases in this category revealed the following interesting information:

Every case had had one or more periods of sanatorium treatment prior to coming to Preston Hall as a patient in the first instance. There was only one non-pulmonary case amongst the fifty-six.

No fewer than twenty-one of the remaining fifty-five have never had tubercle bacilli in the sputum, hæmoptysis, or pleurisy with effusion. In twenty cases out of the fifty-five, tubercle bacilli have been present in the sputum as follows: 1 in 1915; 2 in 1916; 1 in 1917; 1 in 1918; 1 in 1920; 1 in 1921; 2 in 1922; 2 in 1923; 2 in 1927; 1 in 1928. In all cases in this

group, therefore, the sputum has been negative for the five years prior to 1933.

Hæmoptysis without tubercle bacilli appearing in the sputum has been a definite incident in the histories of fifteen cases, but no bleeding indubitably of pulmonary origin has occurred in any case since 1928.

Taking this same group as a whole, the X-ray findings are negligible. Small calcified nodes, heavy root markings, and some accentuation of the normal lines of the bronchi in the lower lobes constitute the most important features. It is to be noted that two of the clearest pictures in the group are to be found in patients who had tubercle bacilli in the sputa in 1916 and 1924 respectively.

The time spent in sanatorium treatment before coming to Preston Hall and at Preston Hall, plus the time spent at Preston Hall in the settlement, totals 7,340 months for the group as a whole—*i.e.*, an average of 128·7 months, or *ten years eight and three-quarter months per man* up to September 30, 1933.

Of the fifty-six men in this group a number are of course key-men—*i.e.*, men who have taken special care, and in some instances have special qualifications, to equip themselves for the special work they have been called upon to do at Preston Hall, and whose substitution would be a matter of considerable difficulty if one is confined to the tuberculous population for applicants. That these men are essential for the continuance of the industrial enterprises in the settlement cannot be denied, and the method of dealing with them will be outlined presently. But the proper conception of the Village Settlement is that it is a centre for the medical care and after-care of individuals suffering from tuberculosis in a degree which precludes their taking part in ordinary industry. Strictly speaking, those cases which can be labelled " arrested " are no concern of the Village Settlement; they are not even the concern of the tuberculosis dispensary. They are far less likely to be " victimised " by outside employers than the patient who is discharged time and time again from sanatoria and who has never had an opportunity of living under the ideal hygienic conditions of the settlement. A man who has maintained an arrested lesion for a period of five consecutive years is, from all points of view, in an infinitely better position than the patient who has just completed a year in a sanatorium, because he has the definite knowledge that the disease is arrested; during the period of his after-care he has had no real financial hardship to undergo; and he has, in addition, been in receipt of a security of tenure denied to the vast majority of consumptives. Further, he is not an infectious individual—an important consideration from the family and public health standpoint.

There is little doubt that in the great majority of cases of pulmonary

tuberculosis which have had five years without symptoms or signs of active tuberculosis the liability to relapse is very slight. Through the kindness of Dr. Lissant Cox I have been able to procure the following figures:

Year.	*Number of Tuberculous Cases written off as Recovered.*	*Number of Recovered Cases restored to Registers.*
1927	975	16
1928	851	36
1929	631	26
1930	876	39
1931	898	44
Total	4,231	161

That is, the number of recovered cases restored to the dispensary registers is only 3·8 per cent.; these are, of course, cases which have *not* received the benefit of Village Settlement life. In a series of 2,488 cases removed from the tuberculosis dispensary registers in two successive years in the London County Council area, the number of cases restored to the registers was 98, or 3·9 per cent.—a figure which is almost identical with that given by Lancashire.

If the Village Settlement at Preston Hall has proved anything at all, it is that after-care of the most comprehensive kind can assist materially in bringing subacute disease to a state of quiescence, and ultimately to arrest. It can also keep a pulmonary lesion in a state of arrest for a period of five successive years. But to keep an arrested lesion in a state of permanent arrest is not a contribution to active treatment, more particularly when we realise that by keeping such cases in the settlement there is likely to be complete stagnation in the flow of new patients into the settlement—cases which are, in fact, suffering from disease which requires prolonged treatment and after-care. No new cases can be taken into the Village Settlement so long as places are being occupied by a group of men for whom there are no longer any medical grounds for continued residence in the settlement.

Either the Village Settlement is a centre for treatment or it is not. If it is to be regarded as a centre for the *employment* of people who have at one time or another been notified cases of tuberculosis, but who are now as nearly healed as it is possible for them to be, then it ceases to be the valuable medical instrument which it now professes to be. Such a policy is not a contribution to the public health principles of our time. We are, by adopting it, merely running workshops for the benefit of a small proportion of people for whom work may be desirable, but not a medical necessity.

Key-men must at all costs be retained so long as their services are required, even if the tuberculous process is arrested. These form the nucleus from

which the settlement as a whole must continue to expand; but even in their case some form of substitution must be found.

In considering so radical an alteration in policy as the one I have just outlined, the viewpoint of the patient who is admitted to the sanatorium, and more particularly the opinion of the Tuberculosis Officer who sends the patient, are well worth considering. New cases have in the past been admitted to the sanatorium section of the settlement full of hope and expectation. They see the settlement light shining brightly, and they cannot help seeing the excellent facilities given to the settlers in their homes and in the workshops. After some months the patient asks: " If I am a suitable case for the Village Settlement, medically, technically, and temperamentally, why should I be shut out when you have men still in the village occupying houses and who are no longer suffering from disease which is likely to relapse ? I have no special desire to remain here for ever; I merely want to get well, but I know that the chances of my recovering fully are remote unless I am allowed to live and work under the sheltered conditions which you have here."

That in a nutshell is the patient's attitude. The Tuberculosis Officer, however, is more to the point. All he says is: " You are keeping a number of men at the Village Settlement who, on purely medical grounds, ought not to be there, and I have no opportunity of getting further men settled unless additional vacancies are provided. Therefore, from the settlement standpoint, there is little encouragement for me to send more patients."

I am strongly of the opinion that the Village Settlement must never take up the rôle of an employment bureau for cases which have once been tuberculous and who merely seek employment. Its function is to care for the sick or the potentially sick.

I regard any scheme by which a man may have five years' security in employment and residence in a hygienic environment with the prospect of arrested disease as the nearest approach to successful treatment which is known, because it restores him to " as near his normal activity as possible."

This is the standard laid down by the Ministry of Health and acted upon by local authorities all over the country. Further, it is the standard set by the Medical Director of Papworth Village Settlement as far back as 1923, when he said in his annual report: " Treatment cannot be termed completely successful if, at the end of it, we have an individual restored to an environment in which the majority of healthy people live, but who is unfit for that environment."

In a more recent report (1933) Sir Pendrill Varrier-Jones has said: " There can be no ' stay too long ' in the case of those persons with permanently damaged lungs, in those who have from time to time exacerbations of the

disease, and who consequently at such times cough up immense quantities of bacilli. Village Settlements are designed for such cases: those very people who are such a problem in the outside world and, indeed, are the problems of the ordinary sanatorium. Those whose sputum was once, and once only, positive when in the army, and in whom the bacilli have never more been demonstrated, are, to my mind, in an entirely different category, and those persons should not be classified with those for whom the Village Settlement is intended. To all intents and purpose they are fit persons and are certainly no danger to the community. *There should be no place for them in the Village Settlement.* (The italics are mine.—J. B. McD.) But for the non-arrested tuberculous there is no more ideal place for treatment and after-care than the Village Settlement, and no more ideal place for the family, remembering always that the family is the unit to be dealt with, and that we waste time and money unless our work centres round this unit."

But in his Mitchell Lecture for 1927 Sir Pendrill has made this important statement: " During the past ten years we have treated 1,778 cases in the sanatorium at Papworth. Those patients who have suitable homes to which to return and who are looked after by the After-Care Association in Cambridge as to their employment are discharged *if the disease is sufficiently arrested.*" If such a principle is sound for patients—and it is a principle generally agreed upon—I cannot bring myself to believe that there should be one principle for patients and another for settlers who come clinically under the same category.

The points which I am stressing are not new. They were expressed in the Report of the Joint Tuberculosis Employment Committee in 1930.

" There are no detailed figures available from Papworth," said the report, " but the Medical Director of Preston Hall is certain that a number of men employed there at present, and who have been in residence for ten years or more, have now reached a stage of arrest and are comparable, medically, to the large group who are, from the clinical standpoint, amongst those normally absorbed into industry. We are of the opinion that ways and means should be devised for the substitution of such cases by others for whom such prolonged treatment under ideal hygienic conditions is so necessary."

Medical men will no doubt recall the wise words spoken by the late Dr. Stanley Tinker on this very subject. " I do not," he said, " advocate over-assistance, pampering, or too much interference. Help the man to help himself; be at his back for a time. As time progresses further conquests will be won."

For the past eighteen months we at Preston Hall have introduced this very system of substitution which was recommended by the Employment Committee of the Joint Tuberculosis Council. It has not, of course, been

an easy task, but its accomplishment has been rendered less difficult by the wholehearted co-operation of the very men in this group who have been amongst the first to recognise the legitimacy and soundness of the proposals.

Fortunately, the British Legion has been of great assistance to many men. Certain financial grants have been made to those who desired to return to their former places of residence and for those who preferred to take up new businesses in other districts. Even the key-men were invited to select houses outside the confines of the Village Settlement itself, and so make way for the placement of new families in the village at Preston Hall.

Nothing in my experience of Village Settlement administration has surprised me more than the anxiety shown by the great majority of the men to fall in with the new order of things.

The administration at Preston Hall has assisted a certain number to obtain alternative employment, and in three cases where this was found the men refused to accept. These men were summarily dismissed from Preston Hall Industries and their houses taken over; in addition, they were given no grant of any kind for their future welfare. The growth and development of the industries at Preston Hall has made it possible for us to absorb a number of arrested cases who are not even key-men, and houses outside the village have been found. There has been ample work for all in the industries. By the middle of 1936 I expect all arrested cases will have left the Village Settlement, and such new cases as may be added to the list with the passing of years will also be removed.

The immediate effect has been most encouraging. New patients admitted to the sanatorium have now a much better opportunity of taking up residence in the settlement, although the demand for places still far exceeds the supply of houses. Just how the Village Settlement conception is to enlarge on the basis of local authority co-operation still remains the major problem for solution. In a future communication I hope to suggest at least one method by which this most desirable of all objects may be fulfilled in some degree.

THE INFLUENCE OF HIGH ALTITUDES ON GENERAL HEALTH AND RECONVALESCENCE AFTER ACUTE ILLNESS

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During the last eighty years mountain climates have steadily attracted more and more attention to their physiological action and to their influence in modifying disease. In tropical countries the hills have always offered a place of refuge from the heat of the plains, and a recruiting ground where ailments contracted in the lowlands could be shaken off. Jourdanet, who practised in Mexico, and Archibald Smith, who practised in Peru, both noticed the comparative rarity of phthisis at high altitudes, and the frequency with which people coming from the lowlands recovered in the mountains from the disease. Rüedi, Spengler, Lombard, and others made the same observation in Switzerland. The consequence has been that mountain resorts have steadily gained in favour for the treatment of certain morbid states. Chief amongst these are tuberculosis, both pulmonary and surgical, certain disorders of the blood and of metabolism, asthma, cases requiring rest under medical supervision—*e.g.*, in convalescence after illness, anæmia, debility or neurasthenia. Another cause has contributed to the popularity of the mountains. Healthy persons who come with their invalid relatives are, as a rule, delighted with the brilliant sunshine and the cool air in summer, or with the equally brilliant sunshine and crisp dry air of the winter. Young people usually do extremely well. Older people, from whom more active tissue change would be advantageous, also profit by a stay in the mountains, provided that their organs of animal life—the organs of circulation, respiration, and digestion —are sufficiently vigorous to respond to the call that will be made on them to do more work.

The mountains have a special reputation in the treatment of both pulmonary and surgical tuberculosis, and this reputation is well founded. The disease is less prevalent at high altitudes than in the lowlands of any

country. This has been established by statistics for Switzerland. The last few years careful observations have established the fact that, almost without exception, people suffering from general debility, tropical diseases, especially malaria, and people with chronic skin diseases do extremely well in the mountains.

Within the last eighty years the value of mountian air as a therapeutic agent has become well known. The growth of Davos, Arosa, St. Moritz, Leysin, Montana, and other Alpine resorts testifies to the popularity of high altitudes, both as health resorts and as pleasure resorts, and equally in summer and winter. Each resort has special characteristics. Davos has three classes of visitors. Some seek only health, some only sport, some a change and rest from their ordinary occupations. Davos is well provided with hotels, sanatoria, and boarding-houses.

The sanitary arrangements in Davos are excellent. There is a very modern system of main drainage, and the utmost care has been taken to obtain an adequate supply of pure water.

In regard to the question of infection by tuberculosis at resorts where persons affected with the disease congregate, it may be mentioned that Davos has a unique disinfection law according to which every room vacated by an invalid suffering from any infectious complaint must be disinfected by a public officer. The danger in any case is small, and is practically absent where ordinary care is taken.

The normal working of the body is contingent upon certain meteorological conditions, the medium for which is the air. The air holds gases, dust and moisture. It acts as a vehicle of heat, a modifier of light, and a conductor of electricity. The effects of these varying phases of matter and energy on the human organism are of the greatest interest, and though much yet remains to be discovered, a brief summary of those at present within our knowledge may be attempted in so far as they concern mountain climate. The changes that result from residence at high altitudes have a number of special features.

When climate influences are modified by an increase of altitude, the organism undergoes physiological modifications to meet the new conditions. Subjectively, there is a feeling of stimulation, and the basis of this is probably a series of changes of a functional kind, only some of which are well understood.

In the mountains the barometric pressure is low in proportion to the height above sea-level, and the partial pressure of oxygen is correspondingly diminished. The physiological result is that breathing is deeper, for the pulmonary ventilation has to be increased if the tissues are to receive their proper oxygenation. The tenuity of the atmosphere, combined, indeed,

with other influences, such as brighter light, leads also to an enrichment of the blood, so that there is a greater amount of hæmoglobin in circulation, and a larger number of red corpuscles to carry it. At a height of 5,000 feet, for example, the increase may amount from 20 to 30 per cent. The increase of hæmoglobin and red corpuscles is not an apparent one due to a diminution of plasma, but a real augmentation, and, indeed, it appears from animal observations that the total amount of blood is also increased. The air at higher altitudes is richer in oxides of nitrogen, which may have some beneficial effect on the respiratory tract.

Mountain air is almost free from dust, more particularly when the snow is on the ground, and is therefore less irritant to the respiratory passages. The presence of silica in dusty air has been shown to be particularly deleterious, and, as it were, an activator of tuberculosis. Dust also includes bacteria, and from these the mountain air is almost free.

There is very much less moisture in the air of mountains than at lower levels, and this dry air has a stimulating effect on the respiratory membranes. And again, because of the low humidity, while it is warm in the sunshine it is cool in the shade. The greater cooling of the body by reason of the cold air, and the evaporative power due to its dryness, necessitate a greater production of body heat, and so an increase of metabolism. The cooling power of Alpine air, as measured by the katathermometer, is three times greater than ordinary conditions indoors, and the evaporative power twice as great. The result is that heat production may be raised from 40 to 90 per cent., according to the degree of exposure. Wind leads to still further increase of heat production. The heightened metabolism thus induced leads to a general tonic effect, the appetite is stimulated, and there is a more ample circulation of nourishment to meet the extra demand.

It is well known that the absence of light has a deleterious effect on the human organism. The successful practice of heliotherapy has abundantly demonstrated the beneficial power of the sun's rays, although the more precise nature of their action remains largely to be explained. From a number of causes the heating and lighting powers of the sun are greatly increased at the higher levels. They are rendered more available because they are much less obstructed than at lower levels. Roget stated that at sea-level 32 per cent. of the heating effect of the sun is lost, whereas at a height of 3,000 metres only 11 per cent. is lost.

The low humidity and the comparative absence of dust leave the air purer and therefore more highly diathermanous. Then, again, there is a longer duration of sunshine, especially on the southern slopes of valleys, and especially in winter, owing to the relative rarity of clouds. In winter,

too, the sun's power is greatly enhanced by the reflection of its radiant energy from the snowfields.

Exposure to sunshine has both local and general effects, the most obvious of which are sunburn and pigmentation. The local response of the skin—*i.e.*, sunburn, or erythema solare—is an inflammatory reaction which may be beneficial in some local morbid conditions, but which must always be carefully controlled, since a deep burn may follow an excessive exposure. Like sunburn, tanning is evidence of a heightened metabolism of the skin, and its occurrence is of great practical moment. People vary greatly in their susceptibility to tanning; some entirely fail to tan. It may be said that in general this pigmentation of the skin is associated with a resistance to disease.

Sunlight has a direct bactericidal action, which is utilised in the treatment of superficial infective conditions, and also for stimulation in the healing of wounds and ulcers. It has also an analgesic property of therapeutic importance, and the great warming power of the Alpine sun, while yet the air is cool and evaporative, may be again referred to in its relation to metabolic stimulation. In this condition, too, it may be recalled that exposure to sun and air has a tonic effect on muscle, so that even an immobilised limb does not atrophy as it would when bereft of these influences. This is doubtless to be correlated with the fact that muscle plays a large part in heat production, and the importance of exercise for the same reason is obvious.

Acclimatisation to altitude consists in adaptation to the changed meteorological conditions. Increased pulmonary ventilation, the enrichment of blood, the strengthened action of the heart, and the response of the skin, alimentary tract, and kidneys to the altered metabolic demands, establish the vital mechanism at a new level. Visitors to a height of 5,000 feet seldom suffer much inconvenience, but slight degrees of headache, sleeplessness, lassitude, flatulence, and breathlessness are to be met with sometimes. Such discomforts do not last longer than ten days, if they occur at all. The young, who bear cold better, acclimatise more rapidly and thoroughly than the old.

It is quite an error to think that the climate of the high mountains is advantageous to patients in the winter only. Clinical observations have made it clear to us that the summer is equally good.

Those affected with bronchial asthma derive enormous benefit from a sojourn in the Alps, but a long stay is necessary if permanent benefit is to be derived.

During the Great War many hundreds of patients suffering from malaria and other tropical diseases were treated in the Swiss mountains. Most of

these patients were infected with these diseases when prisoners of war in Africa, and a great number of them showed signs of infection after their return to Europe, probably due to change of climate. Of these patients—over a thousand in number—only the more severe cases were brought to the Swiss Alps, and it was found that a great number of them, although severely and chronically affected, had only very few, if any, further attacks, so that only the secondary manifestations remained to be treated. The quick recovery from complications, such as cachexia with anæmia, malarial bronchitis, œdema, albuminuria, severe loss of weight, frequent weak pulse, even in bad cases, was often very marked.

To summarise, the principal indications for treatment in the high mountains are as follows :

Pulmonary tuberculosis (if not too advanced).
Surgical tuberculosis—*i.e.* tuberculosis of bones, joints, glands and serous membranes.
Chronic ulcers, sinuses, and fistulæ.
Bronchial asthma, anæmia, convalescence after illness.
Debility, nervous conditions.
Malaria and its secondary manifestations.

The mountains are especially valuable for delicate and backward children of the predisposed type, and for children of bad family history, bad development, adenoids, glands, chronic bronchial catarrh and asthma. In these cases the benefit gained is nearly always rapid and gratifying.

INHALATION THERAPY IN PULMONARY TUBERCULOSIS

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Of the many ways by which drugs can be introduced into the body, perhaps that by way of the air passages has received least attention until recently.

By inhalation therapy is meant treatment by inhaling drugs into the respiratory tract, which includes the nose, pharynx, larynx, trachea, bronchi and alveoli of the lung.

Formerly inhalation was confined to volatile substances possessing curative or soothing properties, whereas today the scope of this therapy can

be extended to a large number of chemical medicines, both oily and fluid in consistency.

At a first glance there does not seem to be anything very new in this method. The breathing of moist airs or vapours impregnated with soothing balsams has been a time-honoured method for the alleviation of acute catarrhal infections of the respiratory passages. The smelling bottle in syncopal attacks, the old bronchitis kettle, and the steam tent for croup, the use of such volatile substances as ether and chloroform, to mention only a few examples, are familiar to everyone and are in common use.

Having been successful so far with volatile substances and with gases like oxygen and carbon dioxide, which are, of course, easily inhaled, search was conducted with a view to determining whether or not it were possible to convert some of the denser substances—*e.g.*, oils and fluids—into a vapour form. Then came the sprays, atomisers, and nebulisers for blowing liquids and oils into a fine state of division, and the insufflators for propelling solids in a finely triturated condition into the air passages. All the foregoing measures were successful as far as they went, but on examining the results of the oils it was found that owing to their molecular weight they tended to fall rapidly on the mucous membranes of the air passages, and consequently did not penetrate very far into the ramifications of the lungs. It had long been known as a physical and chemical fact that elements and compounds, when in the finest state of division possible, gave quicker and more satisfactory chemical reactions. Hence the idea of fine subdivision of the particles had a two-fold use : on the one hand, to get deeper into the air passages ; and on the other, to obtain as quick and as potent an action as possible of the drugs on the surfaces of the lung alveoli. As the alveolar surfaces of the lungs are estimated to be at least forty times greater in area than the exterior surfaces of the body, it would seem that if drugs having the forementioned properties could be deposited thereon some benefit might accrue. It was found that drugs could be so deposited and absorbed. It was also established that local treatment to the respiratory passages could best be given by applying drugs which were not absorbed too rapidly. On this account oily substances were often found preferable. Experiments on animals have shown that if the drugs can be atomised sufficiently finely they can be made to reach the alveoli. For instance, in the case of camphor it is found that it can be absorbed by the blood and excreted in the breath, like garlic. The lungs like to absorb substances of the least density ; the less dense the better they are taken into the pulmonary tissues. The hand-sprays dispense oils and fluids in a fine state of division, but where the particles are inhaled they travel only a comparatively short distance along the air passages—probably only as far as the larynx, or at most the trachea.

These atomisers are very helpful for nasal, pharyngeal, laryngeal, and tracheal catarrhs, but will exert little or no effect on bronchitis. Constant use is made of these daily in the sanatorium. They may, however, prove troublesome, since the drugs become deposited in the pharynx and may be swallowed, causing digestive trouble. To obtain the best results the particles must be fine and dense. Even then only 40 to 50 per cent. of the nebulised drug reaches the termini of the bronchi. It was thought that if it were possible to obtain a direct action in the lung it might in some degree act as a useful adjuvant to sanatorium treatment.

With a view to ascertaining the effect of inhalation treatment in pulmonary tuberculosis, a nebulising apparatus called the Apneu (Speiss-Draper) Inhaling Apparatus was hired. This apparatus is mounted on a cubic foot compressed air cylinder. The air, controlled as in an oxygen cylinder, is forced through two phials, one of which is amber in colour and is used to contain the photo-sensitive drugs like adrenalin; the other a white phial of clear glass, accommodates other drugs, either oils or fluids. The compressed air may be forced through each separately or both simultaneously by a special arrangement of valves. The quantity of air in the cylinder and the rate at which it is passing out of the cylinder are registered on two manometers. Each phial contains an atomiser which dips into the fluid in the conical bottom for a short distance. The vapour thus created passes along into a mixing and depositing chamber, almost like a motor carburetter, thence along to the valved face mask which fits comfortably over the patient's mouth and nose.

This apparatus was very satisfactory, and much appreciated by the patients. Encouraged by this appliance, an English model much on the same lines, but more compact and convenient in size, easier to control and more foolproof, was purchased. The phials are smaller and more easily detached for refilling and cleaning. This model, described as the Apneu Collison Inhaler, is mounted as previously described. It has one manometer only, showing the pressure in atmospheres in the cylinder. A single valve dispenses the compressed air in weak, medium, or strong power. A second valve controls the phials, singly or simultaneously, or allows plain air to pass to the mask as required. A rubber storage bag is in this model interposed between the apparatus and the mask. The 40 cubic foot cylinder is convenient for lifting, and when placed in a cylinder trolley can easily be moved to and from the bedside.

As the fineness of the particles is determined by the strength of the pressure, the greater the pressure the finer the particles. A full cylinder gives better results than one that has been in use for some time. The particles have been measured and found to be as small as $\frac{1}{8000}$ inch, whereas

those from the best hand-sprays are computed to measure about $\frac{1}{50}$ inch. The inhalations can be given warm or cold, in large or small doses. The routine has been to prescribe adrenalin put up in the form of adrenalin synthetic 1/1,000 and 1 per cent. anæsthesin. The latter is included to relieve the irritating effect of adrenalin. This nebulised drug may be given weak, medium or strong, according to the needs of the patient, the medium strength usually sufficing. This is continued for three minutes, followed by rest of three minutes. The valve is then switched over to the other phial, which may contain many kinds of oils or other substances—*e.g.*, camphor, pine, cypress, cajuput, thymol, menthol, creosote, etc. Adrenalin dilates the bronchial tubes and reduces congestion. It has been said of it that acting on any part it has the same effect as stimulation of the sympathetic nerve to the part. For this reason it is by far the most effective treatment in an allergic crisis, for it both neutralises histamine in an allergic crisis as well as stimulates the sympathetic—that is, the inhibitory nerve to plain muscles such as those of the uterus, intestines, and bronchi. Camphor stimulates the breathing centres and blood circulation. Pine, cajuput and cypress are very soothing to the inflamed mucous membrane. Thymol and menthol are antiseptic and cleaning, and creosote is a disinfectant. Iodine, ordinarily very irritating, can be given easily in such fine division.

The treatment, which is given when necessary, has been found soothing to the patient, quite safe, very efficient and well worth the time and trouble expended on it. It relieves distress from asthma, bronchitis, larvngitis, pneumonia, and other pathological conditions associated with pulmonary tuberculosis. It has been used daily at the Elswick Sanatorium in cases of pulmonary tuberculosis complicated by asthma; in the mixed infection bronchitis in tubercle for loosening phlegm, draining bronchi and emptying cavities; for relieving nocturnal cough and promoting sleep; after cases of spontaneous pneumothorax to dilate the bronchi and allow the phlegm to escape from the compressing lung; in cases with acute laryngitis; after severe hæmoptysis to clear the lung and prevent inspiratory bronchitis so often occurring. Patients of all ages can take the treatment, but children tolerate larger doses.

Inhalations quickly relieve the broncho-spasm in cases of tuberculosis complicated by asthma. In cases of shock after induction of artificial pneumothorax the adrenalin inhalations have aborted the symptom. The life of a left-sided artificial pneumothorax case, who developed a spontaneous pneumothorax on the right side and was dying from acute asphyxiation, was saved by this apparatus, as it kept her bronchi open until an aspiration could be performed. Since using the apparatus, patients with

advanced tuberculosis do not seem to have developed laryngeal tuberculosis. This may be a coincidence or may be due to the disinfectant and cleaning action of the drugs inhaled.

A typical prescription may be given as follows:

INHALATION PRESCRIPTION.

Inhalant.	*Time (Mins.).*	*Rest.*
1. Adrenalin	3	
2. Rest		Rest.
3. Camphor	3	
4. Rest		Rest.
5. Adrenalin	3	

From this it will be seen that at the shortest about fifteen minutes is necessary for a treatment. Relief from spasm has been obtained in as short a period as one and a half minutes. Usually two treatments during the day and night are necessary. Particularly is the treatment indicated at night when patients are usually more uncomfortable. There is a wide range of drugs from which to choose a suitable medicine, but in practice these will eventually be limited to a few which give the necessary relief to a tuberculous case.

The preparations which have been generally applicable are apneugene, campheugene and thymol. Apneugene is a mixture of synthetic adrenalin 1 : 1,000 and 1 per cent. anæsthesin. Campheugene, which contains camphor 16 per cent., guaiacol 6 per cent., and menthol 8 per cent., is dispensed in three strengths: extra strong, strong and mild. The latter strength has been used. Thymol is a combination of thymol 1 part, ol. cinnamon 2 parts, and oil of cloves 3 parts. The preparations can be obtained from the Inhaling Drug and Apparatus Company, Ltd., 87, Eccleston Square, London, S.W. 1.

Inhalation therapy by this method was found in practice to entail an extra amount of time and labour on the part of a number of the staff, nursing, clerical and outdoor. The constant ordering, exchanging, forwarding, delivering and returning cylinders was expensive. Means were sought to overcome some of these difficulties. Experiments were made with electric pumps and old cylinders, and as a result 40 cubic foot cylinders can now be charged with compressed air in the wards by the nurse in charge of the case.

This means that good pressure can be maintained, assuring a satisfactory nebulisation, and that the treatment becomes very much cheaper.

The cylinder is prepared for use in the following way: The cylinder is taken and at a convenient height an aperture is drilled. Into this is sweated a strong motor tyre valve. A connection with a Michelin motor

pump is made in the usual way and the pump set in action by being plugged into any ordinary wall plug.

It is convenient to charge the cylinder in a side ward, and afterwards to wheel it to where it is required. A few minutes only is necessary for charging, and two or three good treatments can be obtained with this size of motor pump. More powerful pumps can be obtained which would produce a higher pressure in the cylinder and obviate more frequent charging, but these pumps are heavy to carry about and noisy in action.

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CONTRIBUTION TO THE STUDY OF OLEO-CHRYSOTHERAPY

One Hundred Cases of Pulmonary Tuberculosis treated in a Sanatorium by Suspensions of Gold Salts in Oil

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TEN years have elapsed since Mollgaard presented to the Danish Society of Clinical Medicine the results of his preliminary investigations on the double thiosulphate of gold and sodium. The advent of sanocrysin was greeted with unbounded enthusiasm: it was hailed as the specific remedy for tuberculosis. Unfortunately, these great hopes were soon doomed to disappoint-

ment. Chrysotherapy had only a passing fame, and fell soon enough into disrepute, for serious, even fatal, accidents gave rise to apprehension, and the brilliant results of the Danish pioneers were not confirmed. Nevertheless, the influence and the scientific integrity of the protagonists were to overcome this initial reaction of scepticism and unbelief. In the experimental sphere, as in the clinical, research was resumed, and new supporters of the method arose in all countries. Opponents, however, remained numerous. Contradictory observations flowed in on all sides. Indications and contra-indications, dosage, accidents, results, were the subject of endless study. Finally, reinstated a few years ago by certain experts whose opinion is law, chrysotherapy has escaped from the confines of specialism and has become popularised. But in spite of this official sanction there is little or no unanimity: opinion remains divided, and today the authorities on phthisis are still split into three camps: those who believe firmly in aurotherapy, those who deny it any action whatever, and lastly the more moderate who allow it only a subordinate rôle—as an accessory form of treatment.

For our part we have used gold salts continually in the treatment of a certain percentage of our patients since 1925: and if we have been sparing of enthusiasm, neither have we given way to discouragement in the face of results which were usually indifferent.

We had noted certain facts, clinical, bacteriological and radiological: certain rare but indisputable successes which allowed us to hope that one day aurotherapy might become to tuberculosis what arsenotherapy is to syphilis. Thus one might have asked whether the efficacy of gold salts was not closely connected with the composition of the preparation, and if one could not come to discover the ideal chemical formula capable of fulfilling the hopes of the therapeutists. Much investigation has been undertaken in this direction, and it is still being patiently followed up at the present time.

Up to now the laboratories have placed numerous gold preparations at the disposal of the clinicians. There are too many to choose from. On the one hand, the inorganic salts, the chief being the double thiosulphate of gold and sodium, called sanocrysin. On the other, the groups of organic salts, those now most in use being krysolgan, allochrysin, triphal, lopion, myoral, solganal, and solganal B. Finally, a third group included the more complex salts in which gold is associated with another metal or metalloid: such are neocrysol (gold and arsenic), aurophos (gold and phosphorus), crysiodal (gold, iodine, calcium). Amongst these numerous preparations, which is the best? It is difficult to say with certainty, but in a general way there is a tendency to abandon the inorganic salts more and more in favour of the organic, which are more active from a biological standpoint, and therefore possess a higher therapeutic value.

While the experts were increasing their investigations in chemistry and in biochemistry, it was the problem of the dosage of the gold salts which was first to claim the attention of the searchers in the clinical field.

The massive doses given in the beginning, and responsible for not a few serious and even fatal accidents, gave way to weak ones frequently repeated; but although this latter method had the advantage of being harmless, it had also the disadvantage of being ineffectual. The *via media* was then chosen, and moderate doses received the approval of the majority for some time.

However, it gradually became clear that the patients did not all react in the same way to gold salts; in other words, gold-sensitiveness varied from one subject to another, and a method was then adopted which seemed more rational than the preceding—viz., that of grading the dose to the individual. This is not to say that it is always easy to fix the optimum dose suited to each special case; indeed, we have no formal tests to determine it accurately, and our usual procedure must thus be tentative. Let us add that gold-sensitiveness can also vary in the same patient, so that a dose found to be effectual during a first course of treatment may become harmful or insufficient when a second series of injections is given.

A further problem also confronted us. In considering the reaction of the diseased organism to gold salts it was soon to be seen that success depended not only on the chemical formula of the preparation and the dose used, but also on the tolerance of the subject to the preparation given. It was thus necessary to find not only a gold salt which would be very active and at the same time of low toxicity, but also a technique of treatment capable of increasing the gold-tolerance of the patient. It is beyond question that Feldt's solganal, and especially his solganal B, has so far best realised the first of these conditions. The latter, about ten to twenty times less toxic than the other gold preparations, has an extremely high therapeutic index, since, experimentally, the difference between the maximum therapeutic dose (*i.e.*, the toxic threshold) and the minimum curative dose (that is, the threshold of efficacy) is as 1 : 75.

Having accepted solganal B as very active, easy to handle and to inject intramuscularly, the clinicians now had to apply themselves to perfecting the technique of treatment so as to increase as far as possible the receptivity of the organism. Since 1931 Mollard, Lebœuf and Blanchard had had the idea of applying in the treatment of phthisis oily suspensions such as were already frequently used by syphilologists, especially with regard to bismuth. These authors thought that the slowed entry, and also absorption, of the chemical agent into the economy, its gradual passing into the circulation, its delayed elimination, and therefore its longer stay in the body, would all

encourage the increase of the patient's tolerance to gold, while reinforcing the therapeutic action of the metal. This method, called " oleo-chrysotherapy " by Mollard, has not greatly modified the problem of gold treatment in tuberculosis, yet it marks an important stage in the evolution of the chemotherapy of this disease. For this reason we thought it interesting and justifiable to study its value objectively.

For three years now we have treated certain of our tuberculous lung cases, numbering actually 100, with the injection of gold salts suspended in oil. This number may appear a small one. Let us say by way of explanation that we conceded, and always have conceded, a large place to collapse therapy, the value of which is no longer contested. Thus we have never treated exclusively by oleo-chrysotherapy patients whom we considered able to benefit by pneumothorax or surgical intervention. On the other hand, neither have we reserved gold treatment for the " bad cases," the incurables. In order to act conscientiously and impartially, it is necessary on the one hand to continue the use of treatment of known value, and on the other to put oneself into the most favourable position for benefiting by a new remedy presumed to be active.

We have had recourse to oleo-chrysotherapy: (1) In all favourable cases appearing to be capable of spontaneous cure, so as to accelerate, if possible, the effects of sanatorium treatment at high altitudes. (2) In stationary cases which have ceased to progress. (3) As an accessory form of treatment where collapse therapy has remained insufficient. (4) For serious cases in which collapse therapy cannot be performed, or has failed. (5) For patients who refuse all intervention on principle.

Technique and Dosage.—We shall not spend time on technique, which is very simple. Solganal B in oil is injected intramuscularly into the upper gluteal region. Care must be taken to vary the site of injection each time, for failing this precaution there is the risk of causing accumulations with the danger of massive resorption. It is therefore important to observe this rule, since one is attempting by means of suspensions in oil to achieve slow and regular penetration of gold into the organism. As regards posology, we seek the optimum dose for each particular case, starting as a rule with 1 or 2 centigrammes and rising progressively at the rate of two injections per week until we have reached the " minimum active dose " (Cardis), which varies in each subject. When this dose has been approximately determined we keep to it, while increasing the number of injections to three per week. We do not proceed to a bigger dose unless improvement flags or ceases. We must also add that in the search for the threshold of efficacy we never exceed the dose of 20 centigrammes per injection, nor a total weekly dose of 60 centigrammes. We remain inimical to big doses

and to treatment by so-called " shock tactics," which seem to us more dangerous than helpful. The total dose for a course of treatment is usually from 3 to 3½ grammes, but it can vary in different cases from 2 to 6 grammes. The interval between two series of injections is usually between two and three months.

Survey of Cases—Results.—Let us state, to begin with, that all the patients under consideration have been treated in a sanatorium at a mountain station. This fact places them in conditions particularly suited to deriving benefit from chemotherapy. Thus the results could hardly be compared with those obtained in the treatment of ambulatory patients in a town. On the other hand, it is relatively unusual in a sanatorium to have to treat patients in the acute stage of their illness, whereas in general practice the doctor is often called in to deal with an active progressive lesion in full swing. This difference, we think, is a cause of misunderstanding in the interpretation of results of chrysotherapy. Acute progressive exacerbations in pulmonary tuberculosis are episodes which we know are generally transitory, and though they leave more or less damage in their wake, they nearly always come to an end spontaneously after a varying length of time. So if a course of gold treatment is undertaken in this acute phase (a permissible therapeutic attitude) and the condition changes for the better, one must take care not to attribute exclusively to chrysotherapy an improvement which could have occurred by itself.

Having made this clear, let us now put forward the results of our treatment of 100 patients with oleo-chrysotherapy.

I. Study of Symptoms taken separately.

(*a*) Temperature.

Cases.	*Temperature.*
52	Normal before treatment.
18	Previously febrile, or sub-febrile, became normal.
8	Previously febrile curve improved.
16	No change.
6	Worse.
100	

Thus in 26 the temperature improved during the course of treatment. This would doubtless have occurred spontaneously in some of these, but in several cases the sudden lowering of the febrile curve, or defervescence coinciding with the first injections of solganal, left little doubt as to the part played by the latter.

(*b*) SPUTUM.

Cases.	*Sputum.*
6	Nil before treatment.
18	Completely disappeared during treatment.
37	Diminished.
29	Unchanged.
10	Increased.
100	

Thus out of 94 patients with sputum, 55 improved during gold treatment. In about 20 of these the influence of chemotherapy was capable of being established with some certainty, either because the sputum—unchanged for months—had suddenly diminished from the start of the injections, or because, in other cases, a slower improvement coincided obviously with the treatment.

(*c*) SIGNS ON AUSCULTATION.

We must first take into account the fact that in the majority of patients subjected to rest cure in a sanatorium the signs on auscultation settle down fairly quickly, and, as previously observed, we have much less opportunity than the general practitioner of witnessing a radical change in this branch of physical signs during the course of gold treatment. Thus the figures in this connection are of little value.

Cases.	
13	Definitely improved during treatment.
31	Slightly improved.
43	Unchanged.
11	Worse.
98	

(*d*) WEIGHT.

Cases.	*Weight.*
48	Increased.
38	Unchanged.
14	Lost.

We may point out that in some of the cases the gold salts, especially in the small doses, had very clearly a stimulating action on the digestive function. As against this, digestive disturbances were sometimes provoked after a certain degree of impregnation with gold, making it necessary to interrupt the treatment.

II. Bacteriological Study.

The disappearance of bacilli from the sputum remains up to now the most certain criterion in judging of the efficacy of a therapeutic method. But even here the figures are only approximate and should be interpreted cautiously.

Cases.		
6	... ...	No sputum before treatment.
7	... ...	T.B. negative.
29	... ...	T.B. positive before treatment, becoming negative, and remaining so up to now.
58	... ...	T.B. positive throughout. Some of these became free from bacilli temporarily, but are now again positive.
100		

Thus out of 87 patients with positive sputum before treatment, 29, or 33 per cent., have become negative. These results, admittedly imperfect, seem to us fairly encouraging on the whole. Even if some of the 29 may have lost their bacilli without the help of gold, we are convinced that the majority have become negative because of it.

III. Radiological Evidence.

Radiological modifications depend both on the anatomical forms with which we have to deal and on the phase of activity at which chemotherapy is brought in. Thus each case should really be well studied in detail. But in order to simplify matters we have considered, without distinguishing between them, the radiological improvements revealed during the course of treatment.

Cases.		
18	... ...	Much improved on X-ray evidence.
24	... ...	Slightly improved.
42	... ...	Stationary.
16	... ...	Worse.
100		

We must add that most of these patients had already derived benefit from a course of sanatorium treatment varying from some weeks to some months, and during which the X-ray picture had already had a chance to change for the better.

IV. Sedimentation Rate of the Red Cells.

Cases.		
44	... ...	Lowered.
39	... ...	Unchanged.
17	... ...	Raised.
100		

V. Attempt to judge the Results as a Whole.

This study of the symptoms taken singly does not enable us to estimate as a whole the benefit drawn by our patients from oleo-chrysotherapy (injection of solganal B in oil). This we have now tried to do, returning without bias to our 100 observation cases.

This time we have taken into account, in each case separately, the different factors contributing to general improvement, and we have endeavoured to extricate the part played therein by the gold salts.

Basing this deeper analysis on 100 observed cases, these are the figures we feel able to provide:

15 patients have apparently reaped much benefit from oleo-chrysotherapy.
35 have profited by it to some extent.
40 have made no appreciable progress whatever.
10 have become worse during the course of treatment.

Out of 100 cases this gives us 50 per cent. of favourable results.

VI. Review of Cases according to Localisation, Anatomical Form, Type of Evolution and Duration of Disease.

TABLE I.

			Results. Favourable.	Nil or Bad.
1. *Pulmonary Tuberculosis:* Uncomplicated	Unilateral	Without cavities	5	4
		With cavities	13	10
	Bilateral	Without cavities	8	1
		With cavities	13	20
2. *Pulmonary Tuberculosis:* Complicated by ulcerative tuberculous laryngitis	Unilateral	Without cavities	—	—
		With cavities	—	1
	Bilateral	Without cavities	1	—
		With cavities	5	3
3. *Pulmonary Tuberculosis:* Complicated by bacillary enterocolitis	Unilateral	Without cavities	—	—
		With cavities	1	1
	Bilateral	Without cavities	1	1
		With cavities	3	9
		Total ...	100=50	+ 50
4. *Bacillary Enterocolitis* ... Type	Toxic		4	2
	Ulcerative		—	8
	Hypertrophic		1	1

TABLE II.

Type.				
1. *Exudative*	Unilateral	Without cavities	2	—
		With cavities	1	1
	Bilateral	Without cavities	1	—
		With cavities	3	2
2. *Fibro-caseous*	Unilateral	Without cavities	1	1
		With cavities	11	7
	Bilateral	Without cavities	4	2
		With cavities	14	27
3. *Fibrous*	Unilateral	Without cavities	2	3
		With cavities	3	2
	Bilateral	Without cavities	4	1
		With cavities	4	4
		Total ...	100=50	+ 50

TABLE III.

Tuberculosis.			*Results.* Favourable.	Nil or Bad.
1. *Progressive or sub-progressive* ...	Unilateral	Without cavities	1	—
		With cavities	2	2
	Bilateral	Without cavities	3	1
		With cavities	6	12
2. *Sluggish* (" torpide ")	Unilateral	Without cavities	4	4
		With cavities	12	8
	Bilateral	Without cavities	7	2
		With cavities	15	21
		Total ... 100=50	+	50
1. Apparently dating from less than one year	Unilateral	Without cavities	2	1
		With cavities	5	4
	Bilateral	Without cavities	1	1
		With cavities	5	4
2. Apparently dating from *less than two* years	Unilateral	Without cavities	1	1
		With cavities	3	4
	Bilateral	Without cavities	3	2
		With cavities	3	3
3. Apparently dating from *more than two* years	Unilateral	Without cavities	2	2
		With cavities	6	3
	Bilateral	Without cavities	6	1
		With cavities	13	24
		Total ... 100=50	+	50

VII. Accidents due to Oleo-chrysotherapy.

Out of 100 patients thus treated we have noted accidents in 34 per cent. These mishaps were always mild, transitory, and had no serious consequences. They yielded either to desensitising treatment (calcium, sodium hyposulphite) or to temporary suspension of the injections. In four cases they made it necessary to give up treatment altogether. Taken separately, these accidents may be classified as follows:

		Cases.
Nausea after injection		2
Gastro-intestinal disturbances (certain of which are only the expression of transient hepatic insufficiency)		7
Skin manifestations due to gold	Erythema	4
	Erythrodermia	3
	Pruritus	1
	Eczema	1
	Stomatitis	4
Mucous membrane manifestations due to gold	Pruriginous erythema of vulva ...	1
	Urethritis	1
Albuminuria		3
Transient rise of temperature (" steeple " type)		2
Transient focal reaction		3
Headaches		2

Of the three cases of albuminuria, one was very slight and fleeting. The other two were noted in patients previously suffering from renal disease. One had traces of albumin and granular casts before treatment. The other had had acute nephritis two years earlier, with prolonged albuminuria.

In the three cases in which we discovered a focal reaction, it took the form of a passing congestion not followed by reactivation of the lesion.

We have never had to deplore the least sign of increased tuberculous activity attributable to oleo-chrysotherapy. The patients whose condition became aggravated during the treatment were already getting worse before the start of injections. Extending processes were in no case accelerated. They simply took their course, and gold therapy was unable to influence them.

As we have already remarked in a previous publication on the same subject, if we compare the accidents due to oleo-chrysotherapy in the limits of our experience with those we observed earlier on *with* aqueous solutions, we can state that they have become less frequent, milder and more transient.

VIII. Indications and Contra-indications for Oleo-chrysotherapy.

These refer to gold salts in general: suspensions of solganal B in oil have added nothing new to this subject, except that, being better tolerated, they can be more widely used.

As regards the indications, the matter can be summed up by saying that all the curable forms of pulmonary tuberculosis are capable of being influenced by gold, which is, of course, far from saying that they should all be thus treated. It would be unjustifiable to treat cases amenable to collapse therapy exclusively by gold, unless the patients were opposed on principle to all intervention. It would be equally wrong to believe that chrysotherapy could completely replace or oust sanatorium and climatic treatment. Up to now the gold salts have proved too unreliable to allow of their being placed independently in the same therapeutic category as collapse therapy and hygieno-dietetic treatment. But they are capable of giving help when these more efficacious methods are unrealisable, and can also be associated with the latter to their advantage.

The contra-indications are: intolerance due to idiosyncrasy, renal and hepatic insufficiency, ulcerative intestinal tuberculosis, and, of course, cachexia. Tuberculous laryngitis should not be classed as a contra-indication unless it is the expression of a cachectic state.

IX. Remarks on the Mode of Action of Gold Salts. Pulmonary Tuberculosis and a Syphilitic Soil.

If it can be demonstrated by experiment that gold salts *in vitro* under given conditions are undeniably bactericidal, this is not the case *in vivo*. In fact, Koch's bacillus is not destroyed by gold in the body. Thus, the bactericidal theory, which was defended at first by certain workers as explaining the therapeutic results obtained with sanocrysin, can no longer be interpreted as a direct destructive action of the chemical product on the bacilli, but as a reinforcement of the natural bactericidal power possessed by certain of the body fluids (blood serum, pleural effusion). However, this theory no longer claims many adherents, and the one most generally accepted today is the catalytic theory, whose most authoritative supporter is Feldt. This worker considers that the protection of the organism against the infections assailing it is chiefly undertaken by the mesenchymatous system through a mechanism which is far from simple. As soon as it enters the body the gold is stored up in the cells and fibrils of the reticulo-endothelial apparatus, upon which it exercises a catalytic action, thus reinforcing the tissue defence. Although this latter theory is an attractive one, we have been struck in the course of our clinical work by the inconstancy of this catalytic action. In other words, we have noted with astonishment that this reinforcement of the organism's powers of defence has been far from showing itself regularly in the lung cases we have treated with gold. How does it happen that robust patients, only slightly affected, may derive no benefit whatever from gold, whereas others, seemingly in a dangerous state, with serious lesions, sometimes obtain unhoped-for results? May it be that the chemical agent acts only upon certain pathological soils? On this subject an interesting clinical observation has claimed our attention for several years. We have noticed that our most striking successes with chrysotherapy have occurred in subjects suffering from active syphilis or old-standing fibrotic specific lesions in congenital or hereditary syphilitic cases. Moreover, it is worthy of note that in these cases the pulmonary lesions were of the fibroid type, often of very old standing, and one knows that it is precisely these forms of tuberculosis which are ordinarily refractory to gold salts. Was this a simple coincidence, or should one rather seek in this fact an argument explaining the variability of results in general? Identical observations having been made and recorded by other workers (Mollard, Sayé, Cordier, etc.) in a number of cases of sufficient moment, it seems beyond question that the association of syphilis and tuberculosis creates a pathological soil which is particularly receptive of gold chemotherapy. But in our opinion these clinical observations become especially

significant when brought into line with experimental facts. It has been actually demonstrated in the laboratory that animals artificially tuberculised gained no benefit from chrysotherapy, whatever the dose may have been, whereas experimental diseases such as syphilis in the rabbit, relapsing fever and streptococcal infection in the mouse, could be cured by a single disinfecting injection of solganal.

Putting the clinical and experimental facts side by side has led us to a hypothesis which we had formulated as follows in a previous study : *Do gold salts act only on tuberculous lesions in so far as these have developed on acquired or congenital syphilitic soil?* There is reason, in fact, for asking whether syphilitic soil does not confer on tuberculous lesions a specialised inflammatory character rendering them sensitive to gold.

We know that the idea of specificity is tending to be profoundly revised. A lesion is no longer considered as a specific inflammatory product due to the specificity of the germ, but as a form of tissue reaction, particularly of certain tissue systems of the body, against the pathogenic agent. The reactionary inflammatory complex of the tissues, notably of the tissues entrusted with defence, can play the same part against *different* pathogenic germs, or vary with regard to *one and the same germ* ; finally, it is able to modify itself in the course of the disease (Ranke's stages in tuberculosis; primary, secondary and tertiary syphilis) in the same subject.

It is thus admissible in support of our hypothesis that syphilis modifies the biological soil, provokes far-reaching modifications in the body tissues and fluids which transform the organism's powers of defence against tuberculosis, and *determines a special form of reaction, a definite type of lesion, one of whose characteristics it is to be sensitive to gold.*

If we have allowed ourselves to raise this problem, it is because it appears capable of grouping the indications for chrysotherapy in tuberculosis on new lines.

In July, 1933, we published a preliminary study on oleo-chrysotherapy : our work on that occasion had reference to some forty cases under sanatorium treatment and observation. Although the number of patients to whom we have applied this treatment is now over 100, and we thus benefit by a more extended view, we shall still refrain *pro tem* from drawing definite conclusions. We shall limit ourselves to noting that our first impressions have been entirely confirmed, and to realising :

1. That oily suspensions (solganal B) seem to act with greater efficacy than aqueous solutions of gold salts.

2. That this method is instrumental in helping to develop an appreciable increase in the gold tolerance of the organism.

IMMEDIATE RESULTS IN ONE HUNDRED PATIENTS TO WHOM GOLD SALTS WERE GIVEN

By HILARY ROCHE,
M.D.(MELB.), M.R.C.P.(LOND.),
Medical Superintendent, British Sanatorium, Montana.

NINETY-ONE were given sanocrysin intravenously, 1 was given oleosanocrysin intramuscularly, 8 were given solganol B oleosum intramuscularly; 57 were males, 43 were females. The average stay including readmissions (11 patients were readmitted) was seven months and one week. The average period of rest before graduated exercise was begun was five months.

Indications for Treatment.

	Cases.
1. "Positive" sputum and some toxæmia,* collapse treatment impossible	44
2. Artificial pneumothorax tried, but impossible, or only partially successful	22
3. Disease in the contralateral lung before, during, or after collapse treatment begun	12
4. Unilateral cases: "positive" sputum and some toxæmia, collapse treatment, not tried except in 3 cases later	19
5. Slight persistent toxæmia with pleurisy with effusion	3

Total Amount of Gold Given.

1 patient had more than 10 grammes (in 3 courses).
8 patients had more than 6 grammes (4 of them in 2 or more courses).
74 patients had between 1 and 6 grammes (most of them about 5 grammes).
17 patients had less than 1 gramme.

Dosage.

Treatment generally began with 0·05 gramme; 0·5 in a single dose was rarely exceeded.

Interval—from 3-5 days; up to a week or longer with doses of 0·25 and above.

* A definitely increased blood sedimentation rate, even in the presence of temperatures and pulse-rates within normal limits, was accepted as evidence of toxæmia.

Complications of Gold.

1 patient had a transient slight icterus after 0·35 gramme had been given. Gold abandoned.
7 patients had " rheumatic " pains in upper and lower extremities.
12 patients had some diarrhœa, in 5 only of whom did it tend to recur.
14 patients had *stomatitis*, in 5 of whom it showed a tendency to recur.
21 patients had *albuminuria* at some time during the course. In 3 cases only was it at all severe, in one of which it persisted for some nine months, and in the other for nearly two years. In most cases, however, there was only a faint trace, and usually it did not show a tendency to recur.
22 patients had various *cutaneous manifestations*: 4 had desquamating eczema; 1 had 2 carbuncles on the buttocks; 1 had herpes zoster followed by varicella; 1 had transient urticarial eruption of the giant type on 2 occasions immediately after the intravenous injection of 0·05 gramme of sanocrysin dissolved in doubly distilled water, but no eruption when calcium gluconate was used as the solvent.
40 patients had *anorexia*, with or without digestive disturbances (there were no cases of vomiting).
47 patients had *slight febrile reactions* following injections, mostly on a few occasions only.

A number of patients complained of *depression* in the latter stages of gold treatment.

Result of Sputum Examination (Ziehl-Neelsen).

	Before Treatment.	*After Treatment.*
" Negative "	6	21
" Positive "	84	41
No sputum	10	38

Effect of Treatment on Temperature and Pulse.

	Cases.
Unchanged within normal limits before and after ..	53
Unchanged, raised before and after	6
Worse after treatment	4
Improved	37

Blood Sedimentation Rate (Westergren Method; Drop of Red Cells in Millimetres in First Hour).

Reading.	*Before.*	*After.*
Normal (4 or under in males, 6 or under in females)	7	56
Under 10	13	19
10 to 19	28	11
20 to 29	12	8
30 to 49	19	2
50 to 99	20	3
100 or above	1	1

Changes in Weight during Treatment (Gain or Loss of 1 lb. or Less considered as Stationary).

	Cases.
Gained	57
Lost	29 (of whom 2 were dieted to lose weight).
Stationary	14

Associated Special Treatment.

	Cases.
Artificial pneumothorax	15
Artificial pneumothorax and phrenic avulsion ..	3
Phrenic avulsion alone	13
Phrenic alcoholisation	1
Apicolysis with wax plugging	2
Thoracoplasty	4

Radiological Changes during Treatment.

	Cases.
Stationary	13
Worse	7
Improved	80

Summary.

Investigation of these 100 cases suggests that gold salts are a useful adjuvant to sanatorium treatment. My experience suggests that the radiological improvement noted in many of the cases would not have been so marked, and certainly not so rapid, if gold had not been used.

General rest, however, must remain the essential basis of all treatment. I consider that this factor—there was an average period of five months' general rest in an average total stay of seven and a half months—accounts in large measure for the immediate good results in the large proportion of patients under review.

The beneficial effect of the combined treatment on the general condition is clearly shown by the fact that on discharge 90 of these patients had temperatures and pulse-rates within normal limits, and 75 of them had a blood sedimentation rate of less than 10 in the first hour (Westergren method).

CONSULTATION

CASE I.

By L. S. T. BURRELL,
M.D.(CAMB.), F.R.C.P.(LOND.),
Physician to the Royal Free Hospital and the Brompton Hospital for Consumption and Diseases of the Chest.

The patient, a married woman of twenty-three, complained of recent hæmoptysis and of being unable to pick up after the birth of her second child six months previously. The elder child was two and a quarter years, and she had soon recovered and kept perfectly well after his birth. Her past health was good and there was no history of any illness apart from childhood ailments, but the family history was bad, for her mother died of pulmonary tuberculosis when she was fifteen and her elder brother died from the same cause two years later.

On examination, moist sounds were heard below the right clavicle, and what appeared to be the beginning of a cavity in the lower portion of the upper third of the right lung was seen by X-ray. There was no evidence of any disease elsewhere in the lungs.

Except for a few days after the hæmoptysis the temperature was normal, but tubercle bacilli in large numbers were present in the sputum. The blood sedimentation-rate was fifteen.

A right artificial pneumothorax was recommended but refused, and so she was advised to have absolute rest in bed for six weeks and then have the position reconsidered. She insisted on being treated at home, but agreed not to see the children or have visitors. Home conditions were good and two nurses were engaged for her. At the end of six weeks the cough and sputum had disappeared, the sedimentation-rate was eight and no moist sounds were heard on auscultation. She was allowed to sit up in bed and have extra pillows, but was kept in bed for a further six weeks before beginning to get up. The importance of sanatorium routine and training at this stage was impressed upon her, but she refused to leave home. The nurses were dismissed after a week or so and she gradually resumed her normal life;

indeed, three months after getting out of bed, she gave a tennis party and actually played herself. The cough and sputum, however, returned and she began to feel more and more tired. The evening temperature varied between 99° and 100·4°. The sedimentation-rate was twenty-seven, and there were now definite signs of a cavity at the right apex with a fluid level shown by X-ray.

She now agreed to go into a sanatorium and have an artificial pneumothorax induced. Owing to adhesions, however, no collapse could be obtained, and it was at this stage that this consultation took place.

The possibilities discussed were:

(*a*) Simple medical treatment, consisting of prolonged rest in bed and possibly sanocrysin in a sanatorium followed by sanatorium regime.

(*b*) Surgical intervention:

Phrenic nerve paralysis.
Apicolysis.
Upper thoracoplasty.
Complete thoracoplasty.

The cavity appeared large and it seemed doubtful if it would heal without surgical intervention. Moreover, her temperament made it difficult for her to lead a restful life; she was full of energy, and it was thought that even if she did undergo a prolonged course of medical treatment, she would precipitate a relapse by doing too much as soon as she was allowed up. On the other hand, there are undoubted objections to surgical treatment in this type of case.

A complete thoracoplasty seemed too drastic, although it was realised that if a partial one was undertaken and there was spread into the lower portion of the lung it might become necessary. It was decided to avoid even an upper stage thoracoplasty at this stage, but to regard it as an operation which would very likely be required at some later date.

Apicolysis was seriously considered, but this operation also was thought unnecessary at the present stage. The simplicity of apicolysis, absence of deformity, and slightness of the shock gives it certain advantages over thoracoplasty, but it means leaving a foreign body in the chest and often fails to close the cavity, so that thoracoplasty becomes necessary later. In this particular case it was thought that should an operation become necessary thoracoplasty would be better than apicolysis.

The next matter to consider was whether she should have simple medical treatment or whether extra rest should be given by paralysing the phrenic nerve. It was agreed that phrenic evulsion should not be done on account

of the probability of future surgical treatment. Phrenic crushing, however, was very carefully considered, but was not advised, as the patient was at that time quite ready to rest completely in a sanatorium, but was most opposed to the operation.

The last problem was whether, in addition to rest with suitable food and abundance of fresh air, any special medical treatment should be advocated. It was decided to increase the rest of the lung by using a seven-pound sandbag at first for a short time and then gradually increasing if it did not upset her. A course of sanocrysin was also recommended, starting with 0·1 gm. and increasing at weekly intervals to 0·25 and 0·5 gm., provided there was no reaction, and giving the latter dose until a total of 4 gm. had been given.

Under this treatment she steadily improved, and after eight months in an English sanatorium she went to Davos for six months. On her return from Switzerland she was free from symptoms, and now two years later she remains fit. There is no cough or other symptom, and although X-ray shows fibrosis at the apex of the right lung, there is no clinical or X-ray evidence of cavity.

CLINICAL CASES

AN INTERESTING CASE OF SPONTANEOUS PNEUMOTHORAX

By Y. G. SHRIKHANDE,
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King Edward VII. Sanatorium, Bhowali, U.P. (India).

N. P. S., a boy of 18, came under my treatment as a private patient in April, 1933. He had signs of active disease in the upper half of the right lung, and there was some evidence of activity in the upper third of the left lung also. After a course of solganal-B oleosum injections, artificial pneumothorax was induced in the right pleural cavity in June, 1933. The patient was admitted to the sanatorium on July 4, 1933. On admission, the temperature ranged between 99° and 101° F., average pulse rate was 115 in the morning. T.B. were present in sputum; blood sedimentation rate was 95 mm. at the end of first hour in a column of 200 mm. The patient received his eighth refill on the morning of July 20, 1933, with the following readings: – 11 – 5, 500 c.c., – 5 ± 0.

The temperature remained as usual on July 21, 1933, till five in the evening, when the patient complained of nausea, bilious vomiting, and pain on the right side of abdomen, and the temperature rose to 103·6° F. at 7 p.m. The next morning the temperature was 101·8° F. and abdominal pain was still present. Blood tests showed leucocytes 26,950, and differential count was polymorphs 88·5, lymphocytes 9, and large monocytes 2·5.

Physical examination showed the presence of metallic breath sounds on the A.P. side and apex beat was much displaced to the left side. Screening confirmed the presence of spontaneous pneumothorax on the top artificial one. On July 22, 1933, 300 c.c. of air were withdrawn and the total amount of air aspirated between July 22 and 31, 1933, was 3,900 c.c. Hypodermic injections of camphor in oil and morphia were given as required. Total leucocyte count on July 25, 1933, was 17,950 and blood sedimentation rate on July 28, 1933, was 105 mm.

The patient subsequently developed purulent effusion, of which 1,000 c.c. was aspirated on August 14, 1933, and 650 c.c. on August 25, 1933. The patient left the sanatorium December 11, 1933, when the temperature ranged between 98° and 99·4° F., T.B. were absent in sputum, and blood sedimentation rate was 89 mm.

The patient returned under my treatment in April, 1934, when I aspirated the pus from the pleural cavity and gave intrapleural injections of sanocrysin in increasing doses. As a result of repeated aspirations and intra pleural injections of sanocrysin it was found that the formation of pus was getting less and less and the lung was showing signs of re-expansion. The patient, however, suddenly made up his mind to go back home. I was later informed that he died of profuse hæmoptysis.

The above case is interesting because it presented symptoms at the time of onset which were referred to the abdomen rather than to the chest. Such cases with atypical symptoms are not very common. Beardsley[1] reported one such case in 1911 and remarked on the rarity of abdominal symptoms in pneumothorax; Burrell[2] saw one case mistaken at first for a perforated gastric ulcer; and Oechsli and Skillen[3] have described a case that was transferred from the sanatorium to a hospital with " acute abdominal trouble." It appears to me that the abdominal symptoms in the case mentioned above were caused by the undue displacement of the diaphragm downwards, while the absence of any appreciable amount of breathlessness might be accounted for on the assumption that the mediastinum was not displaced sufficiently to the other side and the embarrassment of the heart was not great.

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OBITUARY

It is with great regret we announce the death at Zurich on August 2 of Dr. Otto Amrein. He was born in Switzerland in 1874 and educated in that country. As a student he showed great ability, but was himself stricken with pulmonary tuberculosis, and in 1900 started practice in Arosa. When the Altein Sanatorium was opened in 1914 he became medical superintendent, a post which he held until the sanatorium was closed some two years ago. Both at the Altein and in his large private practice he came into contact with numerous British patients, many of whom owe their lives to his treatment. His tact and knowledge of the English temperament made him particularly popular, and his death will come as a shock to a large number of British friends. Dr. Amrein's chief hobby was music, and he himself was a first-rate musician. To his widow and son we offer our deepest sympathy.

MEETINGS OF SOCIETIES

JOINT TUBERCULOSIS COUNCIL

At the May meeting of the Council twenty-two members were present. Mr. Girdlestone's resignation was accepted with sincere regret.

The Employment Committee, which is especially studying After-Care, hopes to submit its report in November, and by that time the Contacts Committee, of which Dr. Hebert is convener, and the Pneumothorax Committee, with Dr. Trail as convener, expect to have their reports ready. Dr. Trail's report, it is expected, will deal with some 4,000 cases with controls, and these are being carefully gone through by an actuary. The Medical Research Council have given a grant of £200 towards this work.

On behalf of the Milk Committee, Dr. Hawthorne reported two outbreaks of scarlet fever due to milk contamination, and also an experiment on feeding which had been proposed in which 2,000 children would be fed on raw milk and 2,000 on pasteurised milk. There were difficulties in the way of the experiment, but it was likely these would be overcome.

Dr. Brand reported that twenty participants had followed the Post-Graduate Course at Victoria Park Hospital from February 25 to March 2. Dr. Peter Edwards had held three courses this year and proposed a fourth from July 2 to 4. Arrangements for the study tour in Denmark were approaching completion, and Brompton Hospital would give a Post-Graduate Course from November 4 to 9.

Post-Graduate Study in Tuberculosis for Nurses was discussed and Dr. Ernest Ward, the Hon. Secretary, reported his visits to the College of Nursing and the General Nursing Council. Professor Jameson and Dr. Heaf promised to review the position further and report to the next meeting.

Drs. Tytler and Peter Edwards also promised a note for the next Council meeting on methods of sputum examination. It was suggested that the gasolene concentration method might prove more efficient than culture, as in 4 per cent. of specimens of sputum containing tubercle bacilli the bacilli were dead.

The secretary was asked to circulate for the next meeting literature on the standardisation of blood sedimentation tests.

REVIEWS OF NEW BOOKS

The Rationale of Chest Radiography.

This interesting booklet, published by Watson and Sons, analyses clearly the various factors determining the quality of the chest radiogram.

It shows in graphic form the loss of definition obtained by using tubes with too broad a focal spot, and emphasises the necessity for employing the rotalix (rotating anode tube) for radiography when high milliamperages are utilised. In the section dealing with the loss of definition due to movement of the patient, those caused by transmitted pulsation from the heart and great vessels are unduly stressed to the exclusion of those caused by poor contact between the patient's chest and the film, and those which may result when the patient is examined in the standing position instead of sitting down. The exposure and distance factors recommended correspond to the output of their condenser set, the principles of which are described.

The set combines the great advantages of a minimum exposure time, irrespective of the size of the patient, with control of the radiographic density by the variation of the kilovoltage alone.

La Radiologie des Scissures Pulmonaires. By H. D'Hour. Paris: G. Doin et Cie. Pp. 179. 75 francs.

The systematic study of the interlobar septa in health and disease might be expected to help clear up certain difficult points in pulmonary pathology. A survey of the anatomical relationship of these fissures forms the first section of Dr. D'Hour's book. Radiological examinations of the living body followed by its reconstruction in the form of models forms the basis of this study. Variations from the normal and the puzzling radiological pictures which may arise from such abnormalities as an azygos lobe are subsequently discussed. The value of the lordotic position in localising shadows which may be interlobar is emphasised, and the conclusion is reached that interlobar pleural effusions are very rare in comparison with encysted fluid originating between the visceral and parietal layers of the pleura. The author also suggests that in the past many pulmonary abscesses were wrongly diagnosed as interlobar empyema, which is now found to be a much more uncommon condition.

The word " scissurite," which has no English equivalent, denotes a dry inflammation affecting either the whole septum or simply its junction with the main pleural cavity. Although usually of tuberculous origin, this form of pleurisy may occur as an evanescent thickening in the course of bronchopneumonia or in a more chronic form in bronchiectasis. The characteristic

line seen on the skiagram makes interlobar pleurisy much more easy to diagnose than a similar thickening of the visceral or parietal pleura. Tuberculous lesions in the lung close to the fissures are common, and when their course is followed they are seen to spread more commonly into the other lung than across the interlobar septum. Such lesions must not be mistaken for thickened pleura, as they tend to be progressive, and unless artificial pneumothorax is induced quickly collapse of the lung will be prevented by adhesions.

Numerous radiograms, clearly reproduced, and accompanied by explanatory line drawing, considerably increase the value of the book; there is also an adequate bibliography.

Inhalation Therapy Technique. By W. E. COLLISON. London: William Heinemann, Ltd. Pp. 77. Price 5s.

This little book starts with a brief account of the history of treatment by inhalation, and then describes in detail the modern apparatus and methods of application.

Suggestions as to treatment in different diseases and the appropriate drugs are given. There is a foreword by Sir Bruce Bruce-Porter, and at the end will be found an excellent list of references to the literature of the subject.

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